P300 TOPOGRAPHIC DIFFERENCES BETWEEN SMOKERS AND NONSMOKERS DURING A VISUAL CONTINUOUS PERFORMANCE TASK

A Thesis

Presented to the College of Arts and Sciences

Drake University

In Partial Fullfillment

of the Requirements for the Degree

Masters of Science

by Susan Law

May 1993

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May 1993

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An Abstract of a Thesis by

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May 1993

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The problem. Nicotine is an acetylcholine agonist that modulates the speed and efficiency of information processing and attention. Recently, P300 event-related potentials (ERPs) have been utilized to examine the effects of nicotine and smoking on brain activity and information processing. These previous results indicate that nicotine decreases P300 latency and increases P300 amplitude, indices which suggest faster and more efficient information processing. Nicotine's effect on P300 topography, to this date, has not been explored.

Procedure. The present study explored the effects of nicotine withdrawal on the latency, amplitude, and more specifically, the topography of the P300 ERP in withdrawn smokers (WS) withdrawn for 12 hours, nonwithdrawn smokers (NWS) and nonsmokers (NS) using a degraded visual continuous performance task (CPT). Signal detection analysis was applied, and behavioral measures of response bias (B"), perceptual sensitivity (A'), hit rate (HR), false-alarm rate (FA), and median reaction time (RT) were examined.

Findings. Withdrawn smokers showed a decreased P300 amplitude relative to the NS and NWS groups, even after smoking. In contrast, there were no P300 latency differences between the three groups. A difference in P300 topography was revealed between the three groups as a group x electrode site interaction using normalized P300 amplitudes. Two behavioral measures differentiated between the three groups, HR and B", where the groups' responses varied as a function of session. Smokers, overall, tended to be statistically more conservative in their responses, preferring to commit the error of "miss" versus "false-alarms" relative to the nonsmokers. Nonsmokers overall possessed higher hit rates than smokers.

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INTRODUCTION
P300

The P300 is an endogenous, positive component of the event-related potential (ERP) which occurs at a latency of 250-500 milliseconds to low probability stimuli and task relevant stimuli (Picton, Campbell, Baribeau-Braun, & Proulx, 1978; Donchin, 1979; Hillyard & Kutas, 1983; Nobilio et al., 1990; McCarley, Faux, Shenton, Nestor, & Adams, 1991). Endogenous brain waves can be elicited by environmental contingencies but can also be emitted in the absence of external stimulation. Their characteristics are partially independent of the physical parameters of the eliciting stimulus and they are important because of their association with an individual's prior experience, intentions and decisions and their systematic variation with task requirements and experimental instructions (Donchin, 1981; Pritchard, 1981; for review see Edwards & Warburton, 1984). Some authors have suggested that P300 corresponds to stimulus evaluation time (Kutas, McCarthy, & Donchin, 1977; Donchin, 1981; McCarthy & Donchin, 1981; Donchin et al., 1978; Donchin, 1984; Pritchard, 1981), whereas others believe P300 is related to a closure of cognitive activity which leads to a decision (Verleger, 1988). In any case, the relationship of P300 to attention and memory processes is well established (Donchin & Fabiani, 1991). The P300 is of maximal amplitude over the central and parietal midline of the scalp (McCarley et al., 1991) and has been shown to be an objective and sensitive measure of sustained attention and information processing (Pritchard, 1981).

Because various studies have shown that scopolamine (a muscarinic anticholinergic drug) suppresses P300, accompanied by memory impairment, P300 is thought to be modulated by cholinergic neurotransmission (Nobilio et al., 1990; Knight, 1990). In support of this, Meador and colleagues (1989) have demonstrated that scopolamine, suppressed the P300, whereas, the serotonergic antagonist, methysergide, did not. Meador et al. (1987) hypothesized that cholinergic circuits or networks, from the septal nucleus of the basal forebrain, trigger or modulate the scalp recorded P300 in humans. McCarley et al. (1991) proposed that the P300

originates from temporal lobe generators, specifically, the posterior hippocampus. Intracranial recordings, lesion studies and scalp topography studies have also suggested that the posterior hippocampus and superior temporal gyrus are neural generators of the scalp auditory P300 (Halgren et al., 1980, Halgren, Stapleton, Smith, & Altafullah,1986; Knight, 1990; McCarley et al., 1993).

P300 latency and amplitude appear to index different aspects of information processing. For example, P300 amplitude has been correlated with probability of occurrence, task relevance, subjective probability, decision confidence, equivocation, resolution of uncertainty, and stimulus incentive value (for a review, see McCarley et al., 1991). P300 latency has been related to increased cognitive demands and speed of stimulus evaluation during detection and categorization (Pritchard, 1981). If the stimulus discrimination is made more difficult, then P300 latency will be prolonged. P300 latency has also been shown to gradually increase with age and is further increased by dementing diseases (O'Donnell et al., 1992; Pfefferbaum, Ford, Roth, & Kopell, 1980, Pfefferbaum, Wenegart, Ford, Roth, & Kopell, 1984; Goodin, Squires, & Starr, 1978). The severity of cognitive decline in dementia and Parkinson's disease is related to the degree of slowing of the P300 latency (O'Donnell et al., 1990; O'Donnell, Squires, Martz, Chen, & Phay, 1987). Prolonged P300 latency has also been shown to occur due to drugs that impair cognition (Callaway, Halliday, Naylor, & Schecter, 1985). For example, scopolamine slowed cognitive processing speed and prolonged P300 latency (Callaway, 1984; Callaway et al., 1985; Hammond, Meador, Aung-Din, & Wilder, 1987; Meador et al., 1987; Meador et al., 1988; Meador et al., 1989), whereas the anticholinesterase, physostigmine, appeared to restore the P300 after being eliminated by scopolamine (Hammond et al., 1987). Decreases in P300 latency, in contrast, appear to be indicative of more efficient neural processing of information (Edwards & Warburton, 1984).

P300 and Nicotine

Cigarette smoking helps to sustain performance on monotonous tasks and to produce absolute improvements in both the speed and the accuracy of information processing. Nicotine

tablets have comparable effects indicating that nicotine is responsible for the improvements in smoking (Wesnes & Warburton, 1984). In general, nicotine is the principle psychoactive agent in cigarette smoking (Henningfield & Jasinski, 1983; Pomerleau, 1986) and is thought to play the major role in the improvements in focused-attention tasks that are produced by smoking (Warburton, 1990). In accordance with this, nicotine has been shown to decrease P300 latency resulting in more efficient information processing (Edwards & Warburton, 1983; Edwards, Wesnes, Warburton, & Gale, 1985). In addition, these studies suggest that the effects of smoking on performance are not simply due to enhanced sensory activity or faster motor output, but rather to more efficient information processing (Edwards et al., 1985). The finding that both speed and accuracy improve with the administration of nicotine is important because it shows that there is no speed-for-accuracy trade off (Warburton, 1990). Warburton and Wesnes (1984) hypothesized that the release of acetylcholine (ACh) at the cortex increases the P300 potential amplitude. Therefore, nicotine (because it stimulates the release of ACh) should increase P300 amplitude as well. In contrast, nicotine withdrawal is thought to decrease cognitive efficiency due to reduced ACh release, resulting in decreased cortical arousal, decreased P300 amplitude and increased P300 latency.

Correlations of Nicotine and Acetylcholine (ACh) with Information Processing

Nicotine readily penetrates the brain through the blood-brain barrier, where it acts on nicotinic cholinergic receptors (Pomerleau & Pomerleau, 1984; Benowitz, Porchet, & Jacob, 1990). Nicotine is structurally similar to the neurotransmitter ACh, precisely mimicking it (Domino, 1986), and is thought to influence both parasympathetic and sympathetic activity; most of its influence acts sympathomemetically. Nicotine activates the sympathetic system by releasing norepinepherine (NE) from the postganglionic sites and epinephrine from the adrenal medulla (Pomerleau & Pomerleau, 1984; Benowitz et al., 1990).

There are several extensive reviews linking cholinergic mechanisms with learning, attention, and memory (for a review see Warburton, 1990). In general, cholinergic antagonists

(e.g., scopolamine - a muscarinic receptor antagonist, mecamylamine - a nicotinic antagonist and alpha-bungarotoxin) tend to impair learning and interfere with attention, whereas, cholinergic agonists (e.g., carbamylcholine - a cholinergic agonist, DMPP- a nicotinic agonist, choline acetyltransferase - an ACh synthesizer, and the cholinesterase inhibitor, physostigmine) facilitate acquisition of information (Pomerleau & Pomerleau, 1984; Warburton, 1990). Nicotine, being an ACh agonist, is also thought to facilitate attention and learning (Warburton, 1990).

Deficiencies in the central cholinergic activity have been associated with human attentional and memory disorders such as Alzheimer's disease (Pomerleau & Pomerleau, 1984; Knight, 1990; Sahakian, Jones, Levy, Gray, & Warburton, 1989; Kellar & Wonnacott, 1990). Both human and animal studies have shown that ACh functions as a neural modulator in the hippocampus, permitting efficient functioning of the intrahippocampal circuitry for memory (Knight, 1990; Edwards & Warburton, 1983; Golding, 1988; O'Connor, 1982; Cinciripini, 1986). Degeneration of the nicotinic and muscarinic cholinergic receptors have been associated with Alzheimer's dementia (AD), and administration of nicotine has improved cognitive functioning and attentional processes in patients with AD (Sahakian et al., 1989; Kellar & Wonnacott, 1990).

ACh is also important for many pathways in the arousal system, which extends through the reticular formation to the cortex. Noradrenergic pathways, essential for arousal and alertness, are also modulated by nicotine (Pomerleau & Pomerleau, 1984). Because nicotine alters the bioavailability of endogenous neuroregulators, such as ACh and NE, the drug is thought to be used by smokers to regulate attentional and arousal systems. Nicotine has been shown to facilitate and sustain performance, especially on monotonous tasks, producing improvements in both speed and accuracy of information processing (Wesnes & Warburton, 1983). Moreover, carbamylamine has been shown to increase stimulus detection (Warburton, 1972), while mecamylamine blocks the EEG-activating effects of nicotine in cats (Domino, 1967; Hall, 1970).

Nicotine Receptors and Binding Sites

Nicotine acts both peripherally and centrally and is primarily excitatory (Clarke, 1990). Central nicotinic receptors have been characterized as being pharmacologically similar to the ganglionic (C6) type peripheral receptors (Clarke, 1987; for review see Wonnacott, 1990). Various nicotinic antagonists have been utilized in iontophoretic studies of the CNS: 1) alpha-bungarotoxin and decamethonium - selective for peripheral C10 (muscle endplate) receptors, 2) d-tubocurarine and dihydroßerythroidine - potent at both C6 and C10 receptors, and 3) mecamylamine, hexamethonium, and chlorisondamine - which act selectively at C6 receptors (Clarke, 1990).

The density of receptors on the cell membrane is an important factor in determining the CNS individual neuron responsiveness to iontophoresed nicotine (Clarke, 1990). Auto radiographic maps do not actually permit an analysis of receptor density on individual neurons, but demonstrate a rough correlation between [3H]nicotine and nicotinic [3H]ACh labeling and neuronal responsiveness to nicotine. Areas possessing high [3H]nicotine-binding density include: 1) interpeduncular nucleus [IPN], 2) medial habenula [mHb], 3) cerebral cortex, 4) substantia nigra zona compacta [SNC] and ventral tegmental area [VTA], 5) thalamus, 6) dendate gyrus, 7) neostriatum, 8) inferior colliculus, 9) cerebellum, 10) locus coeruleus [LC], 11) hypothalamus, 12) medulla and pons, and 13) hippocampus (Lichtensteiger, Dominiak, Lienhart, & Hefti, 1976; Clarke et al., 1984, Clarke, Schwartz, Paul, Pert, & Pert, 1985; London et al., 1985; Schwartz, 1986). In the hippocampal formation, nicotine sites have been found in CA1 and the molecular layer of the dendate gyrus (Clarke et al., 1985; London, Waller, & Wamsley, 1985; Yamada et al., 1987; for an extensive review on nicotine binding sites see Wonnacott, 1990 and Clarke, 1990).

Chronic administration of an anti-cholinesterase in rats has resulted in decreased numbers of [3H]nicotine binding sites in the brain (Costa & Murphy, 1983). This down-regulation of the [3H]nicotine binding sites was thought to arise from the increased synaptic availability of ACh after cholinesterase inhibition (Wonnacott, 1990).

Up-regulation of brain [3H]nicotine binding sites to nicotine has also been documented (Marks, Stitzel, & Collins, 1985; Wonnacott, 1987). More specifically, up-regulation reflects an increase in the number of binding sites without a change in their affinity for nicotine. Contrary to expectations, chronic nicotine tends to cause up-regulation of cholinergic receptors (Domino, 1986). In mice, continuous nicotine infusions produced an up-regulation of [3H]nicotine binding sites (Marks, Burch, & Collins, 1983). Moreover, an increase in the number of [3H]nicotine binding sites has also been found in smoker's brains relative to non-smoker's brains (Benwell, Balfour, & Anderson, 1988), with up-regulation of [3H]nicotine binding sites most pronounced in the cortex, hippocampus, and hypothalamus (Marks et al., 1985; Marks, Stitzel, Romm, Wehner, & Collins, 1986). In the rat brain, the auto radiographic distributions of [3H]ACh and [3H]nicotine are essentially identical (Clarke, Hamill, Nadi, Jacobowitz, & Pert, 1986). This, according to Domino (1986, p. 871), suggests that "up-regulation of nicotine cholinergic binding sites to chronic nicotine appears to be an established fact, at least in mice and rats".

Alzheimer patients show reduced numbers of high-affinity binding sites for nicotinic agonists in the brain, which parallel the degeneration of cholinergic projections to the cortex and hippocampus (Whitehouse et al., 1986). The most consistent finding in Alzheimer patients is a decrease in nicotinic sites in the cerebral cortex (Wonnacott, 1990). Similarly, significant decreases in nicotinic receptor binding sites have also been found in the hippocampus (Perry et al., 1987). Further, histological and cytochemical studies indicate that Alzheimer's disease selectively affects neurons in several areas of the brain. Neurofibrillary tangles in cell bodies, neuritic plaques in axon-terminal areas, and loss of neurons, the histological marks of Alzheimer's disease, are most frequently seen in certain brainstem nuclei, the basal forebrain cell groups, hippocampus, amygdala, and neocortex (see reviews in Terry & Katzman, 1983; Price, Whitehouse, & Struble, 1985; Price, 1986).

As stated previously, nicotine acts presynaptically to promote the release of various neurotransmitters in many brain regions (Balfour, 1982; Rowell, 1987) especially ACh and NE

(Domino, 1986). In support of this, the nicotinic cholinergic agonists (i.e. nicotine, carbachol, and 1,1-dimethyl-4-phenylpiperazinium [DMPP]) release endogenous ACh from the presynaptic cholinergic nerve terminals rather than stimulating postsynaptic nicotinic receptors (Chiou & Long, 1969; Chiou, 1973). The nicotinic agonist N-methylcarbamylcholine has been shown to increase ACh release from hippocampal and frontal cortical brain slices (Araujo, Lapchak, Collier, & Quirion, 1988). In contrast, presynaptic muscarinic receptors inhibit ACh release (Domino, 1986). Lesion studies have also shown that a significant proportion of [3H]nicotine binding sites are located presynaptically (Schwartz, Lehman, & Kellar, 1984; Clarke & Pert, 1985; Clarke et al., 1986).

EEG and Nicotine

There is considerable evidence that nicotine causes EEG activation in animals (Domino, 1967; Knott & Venables, 1977). Doses of nicotine from smoking are thought to excite nicotine receptors in the mid brain tegmental-neocortical cholinergic pathway (Edwards & Warburton, 1983, 1984) and produce enhanced activity from the activation of the mesolimbic system (Wonnacott, 1990). Nicotine does not seem to act directly on the cortex, but the indirect outcome of activation is, nevertheless, the release of ACh at the cortex (Armitage, Hall, & Morrison, 1968) and the production of cortical desynchronized EEG (Warburton, 1990). Nicotine causes an increase in alertness accompanied by the shifting of EEG activity from high amplitude, low frequency (8-13 Hz) to low amplitude, high frequency EEG (13-20 Hz) (Edwards & Warburton, 1983, 1984; Golding, 1988) consistent with the effects of nicotine as a stimulant (Pritchard, Duke, Coburn, & Robinson, 1991; Pritchard, 1991). Based on this evidence, Warburton (1990) concluded that smoking improves overall attentional processing.

EEG studies, which have examined withdrawal states, also lend support to the idea that nicotine acts as a stimulant. These studies have concluded that a smoking deprived state causes a decrease in peak to peak amplitudes relative to the predeprivation baseline, whereas smoking causes an increase relative to deprivation in peak to peak amplitudes (Woodson et al., 1982; for review, see Clarke, 1990). Thus, nicotine deprivation is associated with cortical slowing (Ulett

& Itil, 1969; Knott & Venables, 1977) and contributes to slow and impaired cognitive functioning.

Visual CPT and Sustained Attention

A visual continuous performance task (CPT) was utilized in this study to measure sustained attention (vigilance). The subject must maintain attention throughout the entire test, as the target stimuli appears infrequently (Nestor, Faux, McCarley, Shenton, & Sands, 1990; Nestor et al., 1991). Because of its ability to measure sustained attention, the CPT is the most commonly used attentional measure to examine drug effects (Rosvold, Mirsky, Sarason, Bransome, & Bech, 1956; Nestor et al., 1990; Nestor et al., 1991). To test the effects of nicotine on attentional processes, a modified CPT paradigm developed by Nuechterlein, Parasuraman, and Jiang (1983) was incorporated. In this modified visual CPT, the visual stimuli were degraded to decrease signal discriminability and increase error rates; thus, signal detection theory (SDT) was applicable (Green & Swets, 1966; Nestor et al., 1990; Nestor et al., 1991). This vigilance task has been shown to produce rapid declines in perceptual sensitivity over time (Nuechterlein et al., 1983; Nestor et al., 1990; Nestor et al., 1991). Vigilance tasks were recommended for use in smoking studies because many subjects show decreased efficiency over time. Thus, it is possible to show that smoking counteracts decrements in efficiency (Wesnes & Warburton, 1984).

SDT provides measurement of both attention-specific factors (perceptual sensitivity, measured by the nonparametric index A') and nonspecific factors (response bias as measured by B'') (Grier, 1971; Nestor et al., 1990; Nestor et al., 1991). A' is a relatively pure measure of perceptual sensitivity, whereas B'' is a statistically independent index of the nonspecific factors of expectancy, motivation, and/or fatigue. A statistically significant decline in A' over time is rigorous evidence for decrements in sustained attention (Parasuraman, 1984).

Rationale and Hypotheses of Study

Because nicotine is believed to increase cortical arousal by activating midbrain regions (i.e. hippocampus—thought to be a generator of the P300 ERP) and promotes the release of ACh

at the cortex leading to cortical desynchronized EEG, decreased P300 latency and increased P300 amplitude; it seemed plausible that smokers' P300 brain generators would differ from nonsmokers' resulting in P300 topographical differences. Moreover, because nicotine deprivation is associated with the opposite effects, it also seemed plausible that withdrawn smoker's P300 brain generators would differ from both nonsmokers and nonwithdrawn smokers. In addition to examining between-group differences this study also sought to examine changes in withdrawn smokers pre- and post-smoking, testing whether P300 components would normalize after smoking.

This study will examine CPT performance in three groups: nonsmokers (NS), nonwithdrawn smokers (NWS), and withdrawn smokers (WS). It was predicted that, relative to both NS and NWS groups, the WS group would exhibit (as measured at the midline electrode sites of Fz, Cz, Pz): 1) a statistically significant decrease in P300 amplitude, 2) a statistically significant increase in P300 latency, and 3) a change in topography for the midsagittal and midcoronal electrodes during the computerized visual attention task (direction unknown). Moreover, it was hypothesized that the WS group's P300 amplitude, latency and topography would normalize following smoking. For the behavioral data, it was predicted that the WS group would exhibit slower reaction times, lower hit rates, and lower A' values relative to the NS and NWS groups. It was further hypothesized that the false-alarm (FA) and B" values would differ in the WS group relative to the two control groups. Again, the behavioral data for the WS group was expected to normalize after smoking. A' was predicted to decline over time for all groups based on the research of Nuechterlein et al. (1983), as was hit rate.

To date, there are no studies to our knowledge addressing the issue of nicotine withdrawal from smoking and visual P300 topography. The majority of electrophysiological work with nicotine withdrawal was done using EEG, but not ERPs. P300 studies, in contrast, have primarily been concerned with measuring nicotine intake (i.e. nicotine gum), as opposed to withdrawal, using auditory paradigms. In 1984, Edwards and Warburton stated that,

> Knowledge of the source of spontaneous EEG rhythms and ERPs is important because we need to know how different brain waves are involved in different brain processes. Topographical mapping of EEG and ERP by multiple site recordings of scalp activity under a variety of stimulus conditions will provide information of primary sources of activity. (p. 118)

This experiment will attempt to fill a void in the literature by examining the relationship of P300 topography and nicotine using a visual paradigm.

CHAPTER II

METHOD

Subjects

Subjects in this study were taken from a pool of approximately 700 introductory psychology students from Drake University and the Des Moines Area Community College. Based on responses to questionnaires described below, specific subjects were assigned to one of three groups: nonsmokers (NS); nonwithdrawn smokers (NWS); and withdrawn smokers (WS) who were withdrawn for 12 hours. The three groups did not statistically differ by age (mean NS = 19.3, SD = 2.0; mean NWS = 20.6, SD = 1.5; mean WS = 20.9, SD = 2.1) and were counterbalanced for school attended. Each group consisted of six females and six males, all of whom were right-handed, with an exception of one subject who was ambidextrous, as measured through self-report and the Edinburgh Handedness Inventory (Oldfield, 1971). All subjects signed informed consent.

Screening of Cigarette Usage The three groups were differentiated based on the results of two questionnaires which the subjects completed in exchange for course extra-credit. The Fagerström Tolerance Questionnaire (FTQ) (Fagerström, 1978) (see Appendix B) served as a measure of the degree to which smokers were physiologically dependent on cigarettes (Fagerström, 1983; Snyder, Davis, & Henningfield, 1989; Jaffe, 1990), with higher scores indicating greater dependency on cigarettes (see Fagerström, 1978;1983 for further review). The FTQ significantly differed between the three groups (F [2, 33] = 58.57, $p < .001$), but did not significantly differ between the two smoking groups (t [22] = 1.41, $p > .10$) as expected. Thus, NWS and WS groups did not statistically differ in physical dependence to cigarettes as measured by the FTQ. FTQ mean values and standard deviations are displayed in Table 1.

Additionally, the two smoking groups did not differ in the average amount of cigarettes smoked per day (t [22] = .363, $p > .50$) nor in the years of cigarette usage (t [22] = .28, $p > .50$). Mean and standard deviation information on cigarette variables are shown in Table 1.

Table 1

Mean Values and Standard Deviations of Cigarette Information for Nonsmoking, Nonwithdrawn, and Withdrawn Smoking Groups Obtained During Screening Session and Experimental Session

	Controls (NS)		Nonwithdrawn (NWS)		Withdrawn (WS)	
	Mean	SD	Mean	SD	Mean	SD
Screening						
Fagerström Score (FS)	0.00	–	6.83	(1.95)	5.67	(2.10)
Amount nic/cig (mg)	0.00	–	0.86	(0.20)	0.89	(0.11)
Amount tar/cig (mg)	0.00	–	11.21	(3.11)	11.79	(2.09)
Number cigs/day	0.00	–	23.33	(7.49)	21.04	(10.84)
Duration cig use (yr)	0.00	–	5.29	(2.46)	5.92	(3.30)
Experimental						
Pre-smoking CO levels (ppm)	0.00	–	19.33	(10.35)	7.17	(3.43)
Post-smoking CO levels (ppm)	0.00	–	26.42	(12.40)	19.58	(8.24)
Pre-smoking SSQ	19.08	(3.87)	25.33	(6.81)	30.58	(5.79)
Post-smoking SSQ	22.92	(4.30)	24.58	(5.98)	25.17	(7.73)
Number cigs/break	0.00	–	1.75	(0.45)	1.96	(0.54)
Number puffs/break	0.00	–	20.75	(6.55)	21.75	(7.02)

Medical History and Illegal Drug Usage No subject in this study had a history of head injury or neurological disorder. Drug and alcohol usage for the three groups are displayed in Tables 2 and 3. Additionally, none of the control subjects reported using any type of illegal drugs at the time of the initial screening. Within the two smoking groups 11 subjects admitted to some recreational usage of illegal drugs (e.g., marijuana, cocaine) at the time of the initial screening (7 WSs & 4 NWSs). Duration of illegal drug usage did not significantly differ between the two smoking groups (t [22] = .05, $p > .50$), and neither amount or frequency of illegal drug usage correlated with the major dependent variables in this study, i.e. P300 amplitudes or latencies. Moreover, an ANOVA conducted on the midsagittal integrated amplitudes (Fz, Cz, and Pz) between smokers (WS + NWS) who used illegal drugs and smokers (WS + NWS) who did not use illegal drugs revealed no significant group differences. Although there is a clear linkage between substance abuse and smoking, to our knowledge, there have been no previous studies on P300 and cigarettes, which have documented current drug and/or alcohol usage of participating subjects.

Table 2

Type, Frequency, and Duration of Illegal Drug Usage for Nonsmokers, Nonwithdrawn Smokers, and Withdrawn Smokers.

Nonwithdrawn Smokers [1]

Subject	Type of Drug	Frequency of Use	Duration of Use
1.	marijuana	once per month	5 years
2.	marijuana	once per year	1 year
3.	marijuana	greater than 1/week	5 years
4.	marijuana	NA	2 years
5.	marijuana & cocaine	NA	4 years
6.	marijuana	NA	2 years
7.	marijuana	greater than 1/week	6 years
		MEAN DURATION =	3.6 YEARS

Withdrawn Smokers

Subject	Type of Drug	Frequency of Use	Duration of Use
1.	marijuana	once per year	2 years
2.	marijuana	once per week	7 years
3.	marijuana	once per year	8 years
		MEAN DURATION =	5.5 YEARS

[1] There were no nonsmokers who reported using illegal drugs

Table 3

Frequency and Duration of Alcohol Usage for Nonsmokers, Nonwithdrawn Smokers, and Withdrawn Smokers.

	Nonsmokers	Nonwithdrawn Smokers	Withdrawn Smokers
Number of Subjects Reported Using	7	11	12
Mean Duration	2.95 years	4.71 years	5.91 years
Duration Range	(0-5 years)	(0-8 years)	(2.5-10 years)
Amount Drinks/Week	2.91	14.75	6.25
Amount Range	(0-12 drinks)	(0-70 drinks)	(1-24 drinks)

Alcohol Information The three groups did not significantly differ in the amount of alcohol consumed per week (where 1 drink = 1 beer = 1 shot = 1 glass wine) (F [2, 30] = 2.39, p > .10). A one-way ANOVA conducted on the duration of alcohol use (measured in years) revealed a group difference (F [2, 31] = 8.04, p < .005). However, duration of alcohol use did not statistically differ between the two smoking groups (t [21] = 1.32, p > .10).

Procedure

Screening Tests Subjects were given a packet of four pages to complete: 1) an informed consent; 2) a code sheet (present for confidentiality purposes); 3) a demographic questionnaire developed by the experimenter (see Appendix A); and 4) the Fagerström Tolerance

Questionnaire (see Appendix B). Before subjects filled out the questionnaires, they were told that it may be necessary to undergo urine and/or blood analyses at a later date. It was explained that these analyses would be necessary to verify self-reported information on drug usage. In reality, the urine/blood analyses were never to be performed on students. This deception was made by the experimenter in an attempt to maximize accurate responding. All subjects were debriefed as to this deception upon completion of the questionnaires.

To protect confidentiality, regarding sensitive topics such as drug usage, subjects were asked to write their name on the code sheet only. The questionnaires that followed contained the subject's unique code without the subject's name. To further insure confidentiality, subjects were given the option to either: 1) not fill out the questionnaires 2) fill out the questionnaires honestly and check off a corresponding paragraph indicating that the information provided was correct or 3) fill out the questionnaires with false information and check off the corresponding paragraph that said the data was incorrect. Finally, the code sheet was shredded immediately following the experiment. In all cases, subjects received extra credit regardless of how they chose to answer the questionnaire.

The third questionnaire that each subject completed was the FTQ. As mentioned previously, the FTQ served as a measure of the degree to which smokers were physiologically dependent on cigarettes (Fagerström, 1978, 1983; Snyder et al., 1989; Jaffe, 1990). Last, subjects completed a demographic questionnaire which was in the form of a self-report. Subjects recorded: 1) their age 2) their gender 3) their dominant hand 4) if they smoked 5) the quantity of cigarettes smoked per day 6) how long they have smoked 7) the average type, duration, and amount of alcohol consumed per week 8) the average type, duration and amount of caffeine consumed per week 9) medical history involving neurological illness, head injury or epilepsy 10) type of medications being used currently and 11) type, duration, frequency, and amount of illegal substances being used currently. Information on alcohol and caffeine was obtained as previous research has shown a moderate to strong relationship between alcohol and tobacco use and tobacco use and caffeine (Istavan & Matarazzo, 1984). Subjects were told that all

of the information provided was confidential and that their responses would not influence grades in any way.

After the questionnaire packet was completed, subjects were informed that they might be contacted for the second half of the experiment, as this session had only been the preliminary screening. It was further explained that the subjects were not required to participate in the second half of the experiment if they did not choose. At the end of the screening session, information was provided by the American Cancer Society about the hazards of smoking. Phone numbers of health agencies were provided for subjects in case there were further concerns about smoking.

Experimental Design The Fagerström score (FS) and cigarette information, obtained during the screening session, were used to categorize subjects into three groups for the EEG experiment: two experimental smoking groups and one control nonsmoking group. The control group (NS) consisted of non-smokers who received a FS of three or less, who had a smoke-free history and did not have a history of drug abuse for any substance as defined by the DSM-III-R manual (APA, 1987). Subjects within the two smoking groups (NWS, WS) were selected from the original subject pool if they had the highest Fagerström scores in the pool, exceeding the 80%ile and reported smoking at least 10 cigarettes per day (range NWS = 10-40; range WS = 10-40).

After the screening questionnaire data had been analyzed, subjects were selected for each group, contacted by phone and scheduled for an EEG lab assessment in exchange for additional extra credit. Every attempt was made to schedule subjects early in the morning at a standard time as was suggested by Wesnes and Warburton (1984). Approximately 90% of the EEG lab assessments took place between 9 am - 11 am, however, due to time constraints and schedule conflicts the remaining subjects were run 11 am -1 PM and 2 PM - 4 PM. Subjects were called at least 12 hours prior to their experiment to remind them of their scheduled lab time. In addition, subjects were told: 1) the specific time that they needed to discontinue smoking/using nicotine 2) that they would receive a 15 minute break approximately 45 minutes into the

experiment, where they could smoke (if applicable) and/or relax 3) wear glasses (if applicable) instead of contact lenses 4) to bring their own cigarettes to smoke and 5) to limit their alcohol, drug and caffeine intake for the 12 hours prior to the experiment (i.e. Knott & De Lugt, 1991; Knott, 1985; Pickworth, Herning, & Henningfield, 1986). Subjects were told that if they did consume the aforementioned substances, they would be required to document the amount, frequency and time taken of each. Subjects were asked to limit coffee intake the morning of the experiment and informed that the experiment, on average, required two hours to complete for which they would receive extra credit.

Upon entering the lab for the EEG, each subject filled out three questionnaire forms: 1) the Edinburgh Handedness Inventory (see Appendix E) to verify self-reported handedness 2) a subjective state questionnaire (SSQ) (see Appendix D) developed by the experimenter and 3) a brief questionnaire which documented any drug usage (legal and illegal) within the 12 hours prior to the experiment (see Appendix C). The SSQ consisted of eight Likert-type scales, in which the subject was asked to respond to the eight descriptors as he/she currently felt. Items on the scale included, "I feel — 'the need for a cigarette,' 'irritable,' 'alert,' 'relaxed,' etc." The scales ranged from "1" to "7", with "1" being "not at all", "4" being "moderately" and "7" being "extremely." Adjectives were derived from the DSM-III-R criteria for nicotine withdrawal (p. 151). Responses on the SSQ were tallied such that a higher total score on the SSQ served as an indirect measure of the nicotine withdrawal state based on the subjects' self-reports. Nicotine withdrawal was defined as:

> [The] abrupt cessation of nicotine use, or reduction in the amount of nicotine used, [following daily use for at least several weeks and] followed by at least four of the following signs: 1) craving for nicotine 2) irritability, frustration or anger 3) anxiety 4) difficulty concentrating 5) restlessness 6) decreased heart rate 7) increased appetite or weight gain (DSM-III-R, p. 151).

It should be noted that changes in performance and mood have been detected in smokers in as little as two or three hours of abstinence for smoking (Warburton, 1990).

Following the completion of the questionnaires, each subject was asked to exhale into a BreathCO carbon monoxide (CO) monitor (Vitalograph, Inc.). Analysis of the subjects' breath served as a control to check compliance with the abstinence instructions. It has been demonstrated that the CO concentration in parts per million (ppm) is directly correlated to the levels of carboxyhemoglobin (COHb) concentration obtained from smoking (Jarvis, Belcher, Vesey, & Hutchison, 1986), and that subjects who have recently smoked have elevated levels of COHb present in their system (Jarvis, Transtall-Pedoe, Feyerabend, Vesey, & Saloojee, 1987). In contrast, exhaled CO falls to very low levels overnight and it is always detectable if a smoker has smoked on the morning of the experiment (Wesnes & Warburton, 1984).

A CO concentration of 10 ppm or less was selected as a criterion for withdrawn smokers to be included in the study. The 10 ppm CO criterion was based upon the work of Jarvis et al. (1987) who found that 95 per cent of nonsmokers were correctly classified using this criterion. Using 10 ppm as a cutoff value, Jarvis et al. (1987) identified 84% of all smokers, 88% of cigarette smokers and 84% of nonsmokers in relation to self-reported smoking status. The authors concluded that,

> Whether a person is a current smoker can be established accurately by objective tests of smoke intake [i.e. the BreathCO by Vitalograph, Inc.]. The few smokers who cannot be reliably identified smoke so infrequently or inhale so little that their habit is of minimal clinical significance (Jarvis et al., 1987, p. 1438).

Nonwithdrawn smokers were required to test over 10 ppm CO and nonsmokers were required to be under 5 ppm (allowing for possible environmental CO measurement and error).

Event-related potentials (ERPs) and behavioral responses were recorded for a degraded visual continuous performance task (CPT). Subjects sat in a comfortable reclining chair, one meter from a Nec Multisync 2A monitor on which a single digit ranging from zero to nine appeared in the center of the computer screen for a duration of 100 milliseconds at a 1/second rate. Each digit subtended a visual angle of 0.6 degrees horizontally and 0.9 degrees vertically. Subjects were instructed to press the response button only for the target digit (0) which was

irregularly interspersed with the other digit stimuli (1-9) with a probability of 0.19. No response was required for nontargets. Subjects were first given 162 practice trials and needed to obtain an accuracy of 80% hit rate and .90 A' or greater in order to proceed to the actual test. The experimenter coached the subjects, as needed, to minimize muscle movement. After training, a total of 486 trials (120 targets and 366 nontargets) were presented in a random sequence for a period of 10.5 minutes. Trials were divided into three, 3.5 minute blocks (162 trials per block) for data analysis to measure performance changes over time. Stimuli were degraded by altering a specific percentage of the pixels in the 36 x 40 array that subtended a visual angle of 1.3 degrees horizontally and 1.5 degrees vertically. Thirty-five percent of the pixels in the degraded condition were altered. A mask remained on throughout the interstimulus interval which varied randomly between 1.1 and 1.3 seconds. Luminance was held constant.

The proportion of hits (correct target detections) and false alarms (FAs) were computed for each of the three consecutive blocks of trials. The hits and FAs were then used to calculate the nonparametric signal-detection measure of perceptual sensitivity (A') and the response criterion measure (B") (Grier, 1971; Aaronson & Watts, 1987; Nestor et al., 1991). Median and average reaction times were also measured for each subject.

Upon completion of the visual CPT paradigm, both the experimental and control group subjects received a fifteen minute break. During this time, subjects in both smoking groups were allowed to smoke until they felt satisfied. Each subject smoked his/her own brand of cigarettes, and the number of cigarettes smoked and puffs taken for each subject were recorded as were the nicotine and tar content of their cigarette brand. The two smoking groups completed the SSQ at the end of their break to indirectly determine to what degree the effects of nicotine withdrawal had been eliminated. A CO monitor then measured the CO content for the smokers' exhaled air after the break to give an indirect measure of nicotine intake (Jaffe, 1990).

The NS group underwent the same battery of tests as did the two experimental smoking groups, received a fifteen minute break to relax following testing, filled out the SSQ at the end of their break and exhaled into the CO monitor. Scalp EEG electrodes remained in place for all three

groups throughout the break. Immediately following the second SSQ, impedance check and CO measurement, all groups completed a second degraded visual CPT paradigm which was identical to the first.

The selection and treatment schedule yielded a 2 X 3 factorial design with two levels of session (pre and post break), and three groups (NS, NWS and WS) with N = 12 in each group (see Table 4). NS subjects and NWS subjects served as controls for between-group comparisons with the WS group. WS subjects additionally served as their own controls for within-group comparisons between the two sessions.

Table 4

Experimental Design for Nonsmoking, Nonwithdrawn Smoking, and Withdrawn Smoking Groups (N = 12/Group) Using a Degraded Visual Continuous Performance Task (CPT) to Elicit P300 Event-Related Potentials

Group	Session 1	Break	Session 2
NS	Visual CPT 1	Rest	Visual CPT 2
NWS	Visual CPT 1	Smoke & Rest	Visual CPT 2
WS	Visual CPT 1	Smoke & Rest	Visual CPT 2

EEG Recording For each subject, a standardized electrode cap with 13 tin cup electrodes was positioned to record ERPs. The Cz, FP1 and FP2 sites were located by precise measurements and the remaining electrodes were positioned automatically at standard relative distances according to International 10-20 placement (Jasper, 1958).

The cap contained the following electrodes: F7, F8, Fz, C3, C4, Cz, T3, T4, T5, T6, and Pz, where: F= Frontal, C = Central, T = Temporal, and P = Parietal. All scalp electrodes were

referred to linked ears. Vertical EOG were recorded using right eye supra- and infra-orbital electrodes. Horizontal EOG were recorded from electrodes at the right and left canthi. Single trial epochs were digitized and stored on hard disk, with archival storage on tape. The electrode impedance was rechecked when each subject returned from the session break to ensure that the electrodes did not move and that the electrode gel did not dry. Electrode impedance was maintained at less that 5 kOhms throughout the experiment.

ERP sampling began 100 milliseconds prior to the stimulus presentation, and the average of this prestimulus established baseline. Single trial epochs were edited by the computer for voltages of +/- 50 μV, to correct for eye artifact. ERP averages were constructed separately for target ("0") and nontarget trials. Within each session, no fewer than 30 trials composed the target ERP average. The Pz electrode, with the largest positive voltage between 270 and 600 milliseconds, defined the P300 peak component latency. P300 amplitude was measured as the peak voltage between 270 and 600 milliseconds. P300 integrated amplitude was measured as +/- 50 msecs the NS's peak amplitude (484 msecs) at the Pz electrode site during the first session. To eliminate amplitude differences which might be interpreted by ANOVA as a source generator-based interaction, amplitude data, when indicated, were normalized at each electrode site in each experimental condition by the vector length of the grand mean amplitudes (McCarthy & Wood, 1985) to produce a mean vector length of one. Vector length was determined by the square root of the sum of squared grand mean amplitudes over all scalp electrode locations.

CHAPTER III

RESULTS

Cigarette Measures

Subjective State Questionnaires (SSQ) Means and standard deviations for cigarette measures can be found in Table 1. A two-factor model ANOVA, with "session" as the within-subject variable and "group" as the between-subject variable, was used. The analysis revealed a main effect of group for the subjective state questionnaires (F [2, 33] = 5.18, $p < .01$). Tukey's HSD revealed that the SSQ in the first session differentiated between the NS and the two smoking groups (NWS and WS groups; $p < .05$). However, there was no statistically significant difference between the two smoking groups . The WS group had the highest score on the subjective questionnaire followed by the NWS and NS groups (Mean scores = 30.0, 25.0, 19.0 respectively). For interpretive purposes, it is assumed that higher scores on the subjective questionnaire indicate relatively greater "anxiety" or "discomfort" in the subject.

The second SSQ (administered immediately after the smokers had come back from smoking) did not differentiate between the three groups; thus, the strong group x session interaction (F [2, 33] = 8.89, $p < .001$). (Mean scores for the WS, NWS and NS groups on the second subjective questionnaire were 25.0, 25.0, 23.0 respectively). It is interesting to note that while the nonsmokers score increased on the second questionnaire, the nonwithdrawn smokers score did not change, and the withdrawn smokers score (after smoking) appeared to decrease.

Number of Cigarettes and Puffs There was no main effect of "group" for either the number of cigarettes smoked or puffs taken on break between the two smoking groups using a two-factor MANOVA analysis (F [2, 21] = .05, $p > .50$). Thus, the two smoking groups did not differ statistically in the amount of cigarettes or puffs during the break (means and standard deviations are displayed in Table 1). The mean nicotine content in each cigarette used on break did not differ statistically between NWS and WS groups (t [22] = .20, $p > .50$), nor did the average amount of tar within each cigarette (t [22] = .30, $p > .50$). Therefore, the two smoking groups

were potentially subjected to equal amounts of nicotine while on break (mean NWS = .863 mg nicotine/cigarette; mean WS = .892 mg nicotine/cigarette; information on cigarette tar and nicotine values were provided by the R.J. Reynolds Tobacco Company and the Phillip Morris Tobacco Company).

Carbon Monoxide (CO) Levels A two-factor model ANOVA, with "session" as the within-subject variable and "group" as the between-subject variable, was used to examine carbon monoxide (CO) levels. The analysis revealed a significant main effect of group for (CO) levels (F [2,33] = 25.77, $p < .001$). Post-hoc follow-up tests using a one-way Tukey's HSD revealed that both NS and WS groups had significantly lower CO levels than the NWS group ($p < .05$); moreover, the WS group's initial CO content did not significantly differ from the NS group. Upon returning from the smoking break, the WS group's CO level did not significantly differ from the NWS group, and both smoking groups' CO levels significantly differed from the NS group ($p < .05$).

Secondly, a highly significant "session" effect was found for the CO variable (F [1,33] = 98.20, $p < .001$), and as can be seen by the values in Table 1, both smoking groups' CO level rose from session one to session two after smoking. Moreover, a significant group x session interaction was found using a repeated measures ANOVA (F [2,33] = 30.74, $p < .001$). As can be seen by the means in Table 1, the WS group had consistently lower levels of CO than the NWS group. For example, in session 1, the NWS group had a mean CO of 19.33 ppm while the WS group had a CO mean of 7.17 ppm. (The WS group CO ppm mean met the 10 ppm CO criterion to be considered withdrawn). After smoking, the NWS group's CO mean rose to 26.42 ppm while the WS group mean CO rose to only 19.58 ppm. In contrast, the NS control group's initial CO concentration was 1.58 ppm and was virtually unchanged following the break at 1.50 ppm.

Behavioral Data

Median Reaction Time (RT) Behavioral and performance measures are summarized in Table 5. (Due to a computer technical error, behavioral data are available for 35 out of the 36 subjects). A three-factor model ANOVA, with "session" and "block" as the within-subject

variables and "group" as the between-subject variable, was used. The analysis revealed a main effect of "session" (F [1,23] = 5.41, $p < .05$) where median RTs were reduced for all three groups in the second session. A statistically significant "session" effect was also found collapsing across three blocks (F [1,32] = 5.74, $p < .05$). No significant "group" or "block" differences were found. There were no significant effects found using average RTs.

Hit Rate (HR) A three-factor model ANOVA, with "session" and "block" as the within-subject variables and "group" as the between-subject variable, revealed that the main effect of "group" was nonsignificant. However, a "group x session" interaction was statistically significant (F [2,32] = 4.73, $p < .05$). Collapsing across blocks continued to produce the "group x session" interaction (F [2,32] = 4.96, $p < .01$), where the NS group had the highest mean HR in session one while the NWS and WS groups' HR was remarkably similar (Mean HR: NS = .820, NWS = .785, WS = .787). During the second session, the NS group again had the highest HR followed by the NWS and WS groups respectively. (Mean HR: NS = .890, NWS = .801, WS = .759). Note that both the NS and NWS groups' HR increased, while the WS group's HR decreased after smoking. Finally, a strong "block" effect was present (F [2,64] = 14.08, $p < .001$) as HR declined over time for all groups in both sessions.

False Alarm (FA) A three-factor model ANOVA, with "session" and "block" as the within-subject variables and "group" as the between-subject variable, revealed a statistically significant "block" effect (Greenhouse-Geisser corrected F [1.94, 62.21] = 10.33, $p < .001$), and "session" effect (F [1,32] = 9.27, $p < .005$). As shown by the means in Table 5, FAs were reduced during the second session across the three groups. Collapsing across the three blocks continued to produce a statistically significant "session" effect (F [1,32] = 16.93, $p < .001$). There was no statistically significant "group" effect for FA. A planned 2-tailed paired t-test revealed that the WS group's FA rate was statistically different between sessions (t[10] = 2.66, $p < .05$).

TABLE 5

Behavioral and Performance Measures for Nonsmoking, Nonwithdrawn, and Withdrawn Smoking Subjects

Group	Session 1 Blocks			Avg. Session 1	Session 2 Blocks			Avg Session 2
	1	2	3		1	2	3	
	Hit rate (%)							
Controls								
Mean	87.3	80.4	77.6	82.0	90.9	87.8	86.3	89.0
SD	(9.7)	(13.8)	(10.3)	(8.4)	(6.4)	(10.6)	(13.1)	(7.1)
Nonwithdrawns								
Mean	86.8	74.2	73.1	78.5	86.4	78.4	74.2	80.1
SD	(8.5)	(18.3)	(17.8)	(13.0)	(10.4)	(15.8)	(18.8)	(12.7)
Withdrawns								
Mean	87.5	77.1	70.6	78.7	81.6	72.8	71.9	75.9
SD	(14.9)	(19.5)	(26.7)	(18.9)	(21.6)	(26.7)	(26.7)	(24.4)

(Table 5 continued)

Group	Session 1 Blocks 1	2	3	Avg. Session 1	Session 2 Blocks 1	2	3	Avg Session 2
False-alarm rate (%)								
Controls								
Mean	7.1	6.9	3.6	5.9	5.9	5.5	4.2	5.1
SD	(4.6)	(5.3)	(2.4)	(3.4)	(5.6)	(5.6)	(3.5)	(4.5)
Nonwithdrawns								
Mean	5.4	6.1	4.8	5.0	5.2	3.1	4.2	3.9
SD	(5.8)	(9.9)	(8.0)	(6.2)	(7.4)	(5.1)	(7.5)	(5.6)
Withdrawns								
Mean	7.2	3.5	2.3	4.5	3.6	1.8	1.4	2.5
SD	(6.0)	(4.1)	(2.8)	(3.8)	(3.6)	(2.5)	(1.8)	(2.4)
Median Reaction Time (ms)								
Controls								
Mean	445	429	449	424	426	420	423	404
SD	(85)	(55)	(56)	(54)	(68)	(52)	(55)	(54)
Nonwithdrawns								
Mean	445	464	454	443	417	435	436	418
SD	(74)	(82)	(70)	(74)	(71)	(71)	(69)	(67)

(Table 5 continued)

Group	Session 1 Blocks 1	2	3	Avg. Session 1	Session 2 Blocks 1	2	3	Avg Session 2
Median Reaction Time (ms) (cont'd)								
Withdrawns								
Mean	451	465	461	449	461	469	477	449
SD	(43)	(43)	(47)	(35)	(65)	(75)	(83)	(69)
A'								
Controls								
Mean	0.99	0.92	0.93	0.93	0.96	0.95	0.95	0.96
SD	(0.00)	(0.05)	(0.03)	(0.03)	(0.03)	(0.03)	(0.04)	(0.03)
Nonwithdrawns								
Mean	0.95	0.92	0.91	0.93	0.95	0.93	0.92	0.94
SD	(0.04)	(0.06)	(0.05)	(0.04)	(0.03)	(0.06)	(0.05)	(0.04)
Withdrawns								
Mean	0.94	0.93	0.92	0.93	0.94	0.92	0.92	0.93
SD	(0.06)	(0.06)	(0.07)	(0.06)	(0.05)	(0.07)	(0.07)	(0.06)

(Table 5 continued)

Group	Session 1 Blocks 1	2	3	Avg. Session 1	Session 2 Blocks 1	2	3	Avg Session 2
	B''							
Controls								
Mean	0.21	0.42	0.63	0.44	0.32	0.22	0.51	0.32
SD	(0.41)	(0.26)	(0.25)	(0.22)	(0.41)	(0.70)	(0.29)	(0.38)
Nonwithdrawns								
Mean	0.42	0.57	0.65	0.61	0.45	0.67	0.69	0.63
SD	(0.34)	(0.42)	(0.33)	(0.32)	(0.50)	(0.36)	(0.44)	(0.41)
Withdrawns								
Mean	0.09	0.57	0.50	0.43	0.46	0.72	0.69	0.61
SD	(0.40)	(0.33)	(0.59)	(0.50)	(0.50)	(0.21)	(0.36)	(0.46)

Note: A' = nonparametric measure of sensitivity; 0.5 = chance performance, 1.0 = perfect discrimination, B'' = nonparametric measure of response bias; low values indicate a more liberal bias, high values indicate a more conservative bias.

A-Prime (A') A three-factor model ANOVA, with "session" and "block" as the within-subject variables and "group" as the between-subject variable, revealed that the main effect of "group" was statistically nonsignificant. However, the main effect of session was present (F [1,32] = 8.00, $p < .01$) where A' tended to increase during the second session as compared to the first session for all three groups. Collapsing across blocks continued to produce the strong "session" effect (F [1,32] = 9.42, $p < .01$), where the NS group had the highest A' in session 1 while the NWS and WS groups had virtually the same A' (mean A': NS = .934, NWS = .927, WS =

.930). During session 2, the NS group again possessed the highest A' followed by the NWS and WS groups (mean A': NS = .956, NWS = .936, WS = .930). Note that as with HR, both the NS and NWS groups' mean A' increased during the second session, while the WS group's A' did not change after smoking. Finally, there was a main effect of "block" (Greenhouse-Geisser corrected F [1.79, 57.22] = 6.00, $p < .01$) indicating that A' tended to decline over time within a session for all groups.

Beta (B'') A three-factor model ANOVA, with "session" and "block" as the within-subject variables and "group" as the between-subject variable, revealed a significant "block" effect (Greenhouse-Geisser corrected F [1.49, 47.81] = 19.30, $p < .001$). Specifically, Tukey's HSD revealed a significant difference in response bias between the NS and WS groups for the second block in session 2 where the NS group was liberal in response (B" = .216) compared to the WS group's conservative bias (B" = .724).

Although the main effect of "group" was statistically nonsignificant, a "group x session" interaction was statistically significant (F [2,32] = 3.91, $p < .05$). A "group x block" interaction was weakly significant (Greenhouse-Geisser corrected F [2.99, 47.81] = 2.59, $p <$ .06). Overall, during session one, the WS group tended to be most liberal responders (mean B" = .430), while the NWS group tended to be the most conservative (mean B" = .606). During session two, however, the NS group became the most liberal (mean B" = .324) while the WS group (after smoking) became the most conservative (mean B" = .628). Collapsing across blocks continued to produce the significant "group x session" interaction (F [2,32] = 3.51, $p < .05$). For both sessions, the WS group had the most conservative response during the second block. In contrast, the most conservative response for both the NWS and NS groups occurred during the third block in each session.

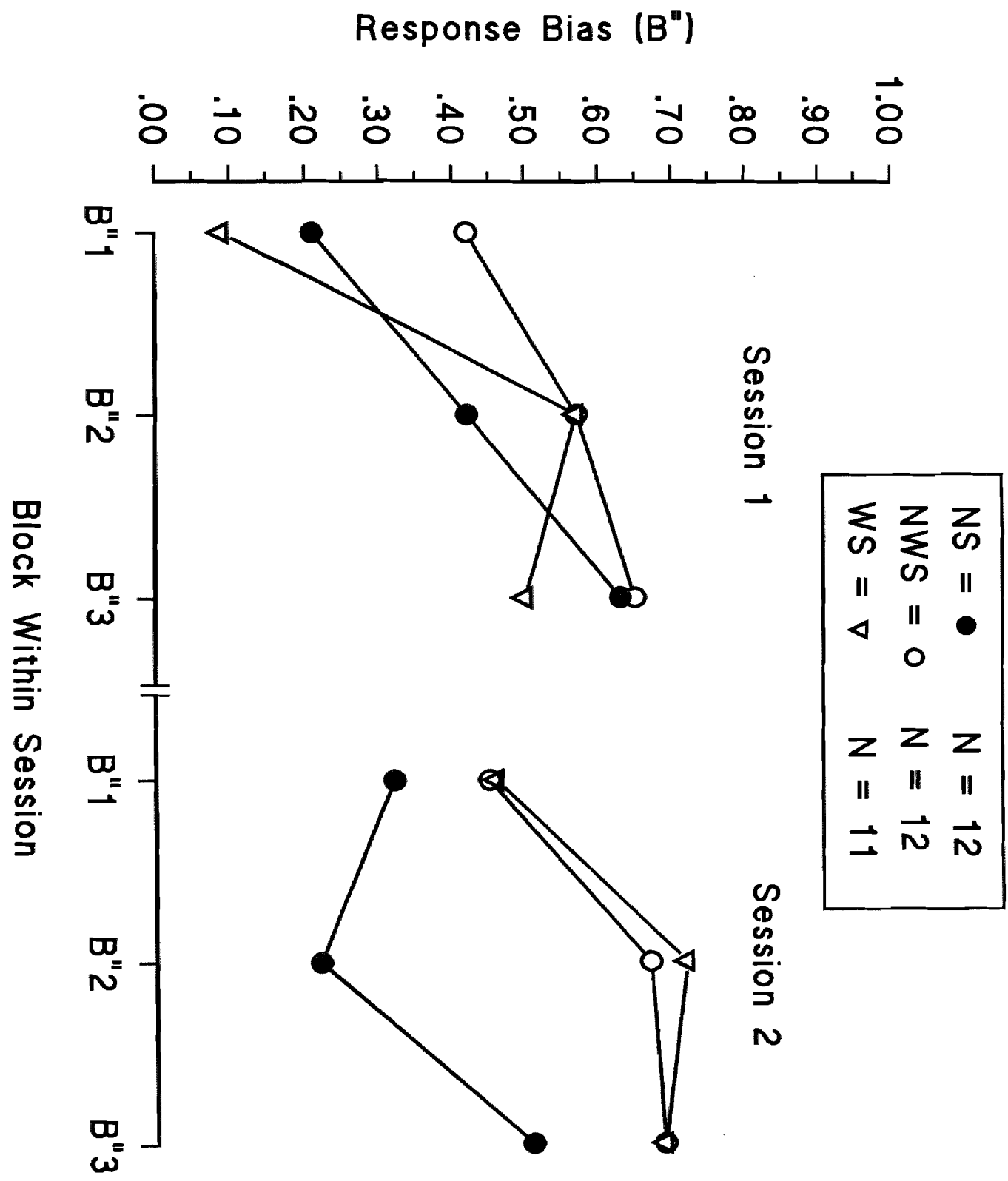

Response Bias (B")
.00
.10
.20
.30
.40
.50
.60
.70
.80
.90
1.00
B"1
B"2
B"3
B"1
B"2
B"3
Block Within Session
Session 1
Session 2
NS = ● N = 12
NWS = o N = 12
WS = ▵ N = 11

Figure 1. Mean Response Bias (B") Values Labeled by Session and Block for Nonsmokers, Nonwithdrawn Smokers, and Withdrawn Smokers.

For clarification, B" standard error values are presented here for each group.

NS	Block 1	Block 2	Block 3
Session 1	.117	.075	.072
Session 2	.120	.203	.084
NWS			
Session 1	.097	.121	.095
Session 2	.144	.105	.126
WS			
Session 1	.119	.100	.179
Session 2	.150	.065	.108

Event-Related Potential Data

P300 Integrated Amplitude Analyses Using Non-Normalized Data Mean P300 integrated amplitudes (434-534 msecs) among the 13 scalp electrodes are presented in Table 6 and Figure 2. Grand average wave forms to the target ("0") are presented in Figure 3. A planned, three-factor model ANOVA was used, with "session" and "site" as the within-subject variables and "group" as the between-subject variable . The analysis revealed a statistically significant main effect of "group" (F [2,33] = 3.53, $p < .05$) as well as a "group x electrode site" interaction (Greenhouse-Geisser corrected F [6.55, 108.11] = 2.95, $p < .01$). Overall, as expected, the WS group differed from the NS group at the most electrode sites using Tukey's HSD post-hoc test. More specifically, the WS group had statistically smaller P300 amplitudes at Cz and Pz midline electrode sites ($p < .05$) relative to the NS group. Interestingly, the NWS had a statistically smaller P300 amplitude at the T6 electrode site ($p < .05$) relative to the WS and NS groups (mean T6 amplitude: NS = 8.53, NWS = 4.07, WS = 7.23).

TABLE 6

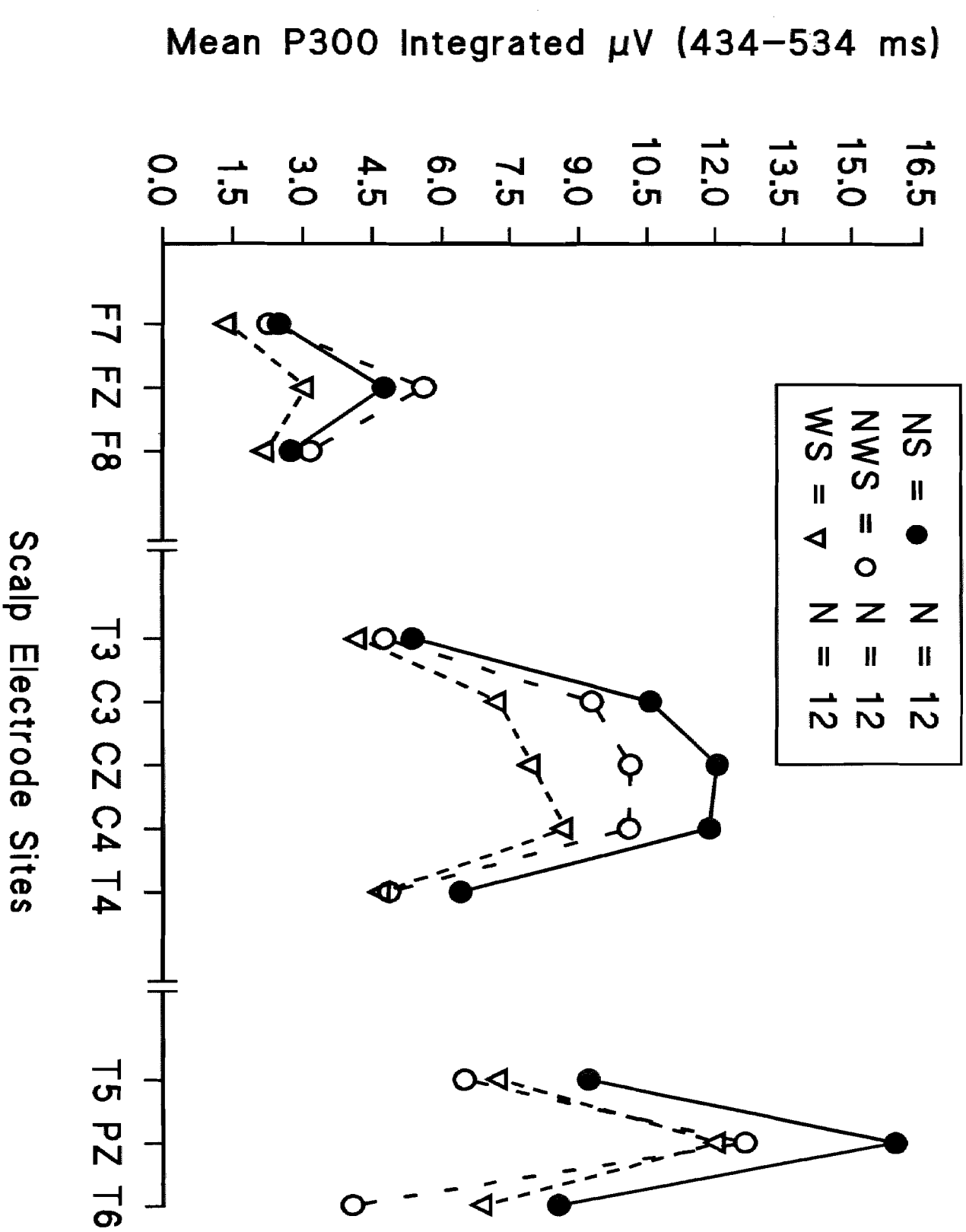
P300 Integrated and Peak Amplitude Values for Nonsmoking, Nonwithdrawn, and Withdrawn Smoking Subjects

Group	Session 1 Sites			Session 2 Sites		
	FZ	CZ	PZ	FZ	CZ	PZ
	P300 Integrated Amplitude (μv)					
Controls						
Mean	4.66	12.07	15.71	4.83	12.00	16.13
SD	(1.70)	(3.09)	(3.14)	(2.00)	(4.19)	(3.84)
Nonwithdrawns						
Mean	5.12	9.45	12.08	6.12	10.83	13.23
SD	(2.73)	(2.88)	(3.46)	(3.24)	(4.20)	(3.40)
Withdrawns						
Mean	2.97	8.16	11.94	3.17	7.84	12.20
SD	(2.71)	(4.07)	(4.45)	(2.82)	(2.62)	(3.24)
	P300 Peak Amplitude (μv)					
Controls						
Mean	6.70	14.61	18.57	7.33	15.54	20.09
SD	(1.86)	(3.60)	(3.95)	(2.40)	(5.01)	(5.12)

(Table 6 continued)

Group	Session 1 Sites			Session 2 Sites		
	FZ	CZ	PZ	FZ	CZ	PZ
	P300 Peak Amplitude (μv) (cont'd)					
Nonwithdrawns						
Mean	7.78	12.85	15.71	9.13	15.11	17.92
SD	(3.88)	(3.86)	(4.07)	(4.85)	(5.13)	(4.16)
Withdrawns						
Mean	5.12	10.43	14.48	5.93	10.90	14.98
SD	(2.81)	(4.13)	(4.22)	(2.98)	(2.51)	(3.35)

The WS group, again, had significantly smaller P300 amplitudes ($p < .05$) relative to the NS group during session 2 at the Cz, C4 and Pz electrodes using a Tukey's HSD analysis. In addition, the NWS group had a significantly smaller P300 amplitude at the T6 electrode site relative to the NS group ($p < .05$), but not to the WS group (mean T6 amplitude: NS = 8.62, NWS = 4.10, WS = 6.71). The NWS group had the largest P300 Fz amplitude, significantly larger than the WS group's Fz amplitude, but not from the NS group's (mean Fz amplitude: NS = 4.83, NWS = 6.12, WS = 3.17).


Mean P300 Integrated μV (434–534 ms)
0.0
1.5
3.0
4.5
6.0
7.5
9.0
10.5
12.0
13.5
15.0
16.5
NS = ● N = 12
NWS = o N = 12
WS = Δ N = 12
F7 FZ F8
T3 C3 CZ C4 T4
T5 PZ T6
Scalp Electrode Sites

TARGET ('0') CONDITION

GRAND AVERAGES (N=12 / GROUP)

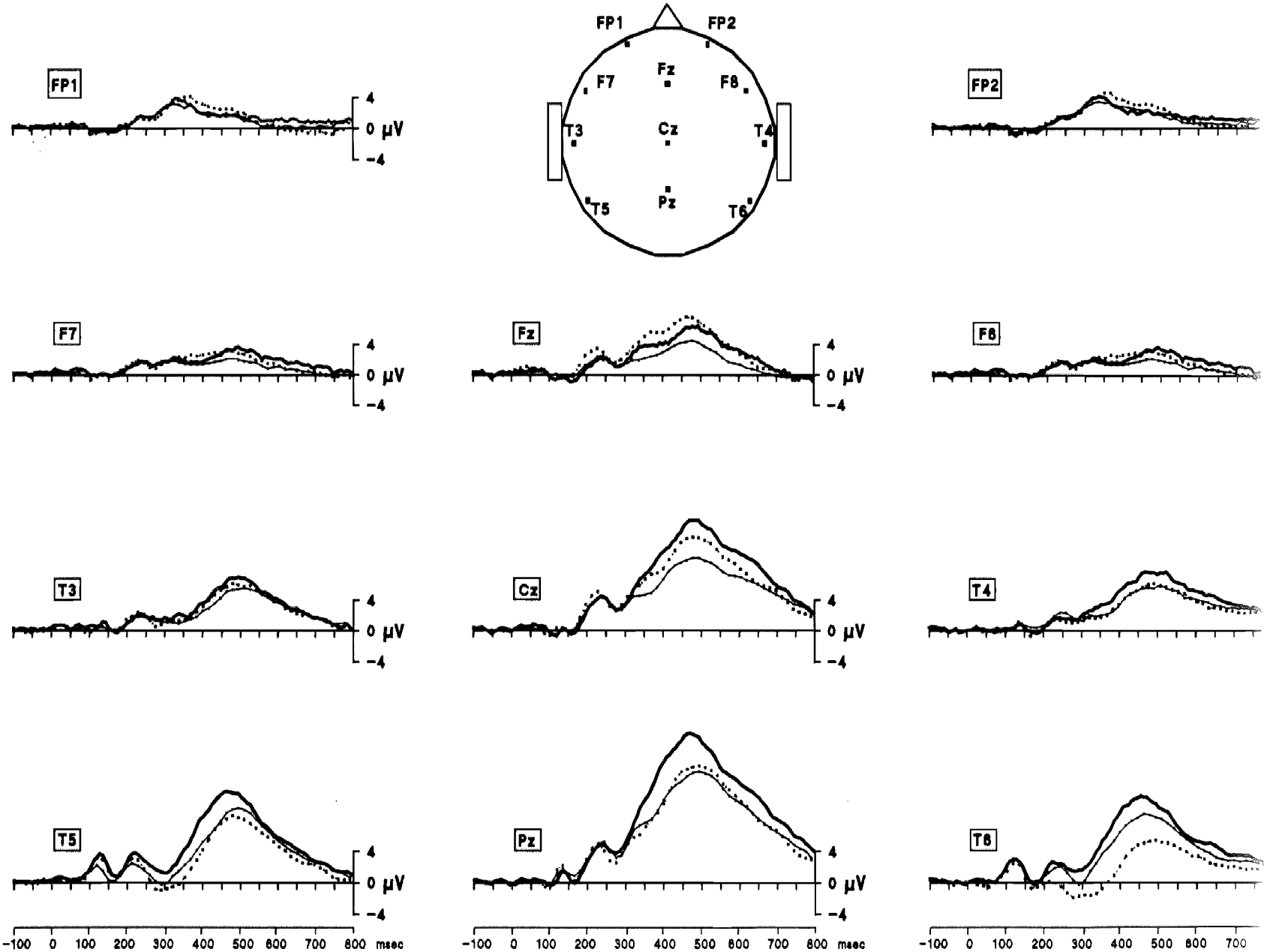


Figure 2. Mean P300 Midsagittal Integrated Amplitude Values Averaged across Session 1 and Session 2 for Nonsmokers, Nonwithdrawn Smokers, and Withdrawn Smokers.

For clarification, P300 integrated amplitude standard error values are presented here for each group.

NS	F7	Fz	F8	T3	C3	Cz	C4	T4	T5	Pz	T6
	2.53	1.49	1.63	2.65	3.92	3.30	2.64	1.53	3.30	3.26	2.16
NWS	F7	Fz	F8	T3	C3	Cz	C4	T4	T5	Pz	T6
	2.18	2.85	2.00	2.10	3.66	3.38	2.59	1.75	2.78	3.27	3.85
WS	F7	Fz	F8	T3	C3	Cz	C4	T4	T5	Pz	T6
	1.76	2.59	2.01	1.68	3.09	3.16	3.22	2.50	1.95	3.72	2.67

Figure 3. Grand Averaged Wave Forms Averaged across Sessions for Nonsmokers, Nonwithdrawn Smokers, and Withdrawn Smokers.

P300 Integrated Amplitude Analyses Using Normalized Data To test for overall P300 topography differences between groups, a three-factor model ANOVA, with "site" and "session" as the within-subject variables and "group" as the between-subject variable was performed using normalized P300 amplitude data from all 13 scalp electrodes. Results are presented in Figure 4. As expected, there was no main effect of "group". However, a "group x electrode site" interaction was significant (Greenhouse-Geisser corrected F [7.64, 126.06] = 2.04, $p < .05$). Using Tukey's post-hoc criterion to test for differences between groups at specific electrode sites, the NWS group had a proportionally smaller P300 amplitude at the T6 electrode site than that found in the WS and NS groups ($p < .05$; mean T6 normalized amplitude session 1: NS = .286, NWS = .174, WS = .326; session 2: NS = .281, NWS = .159, WS = .299).

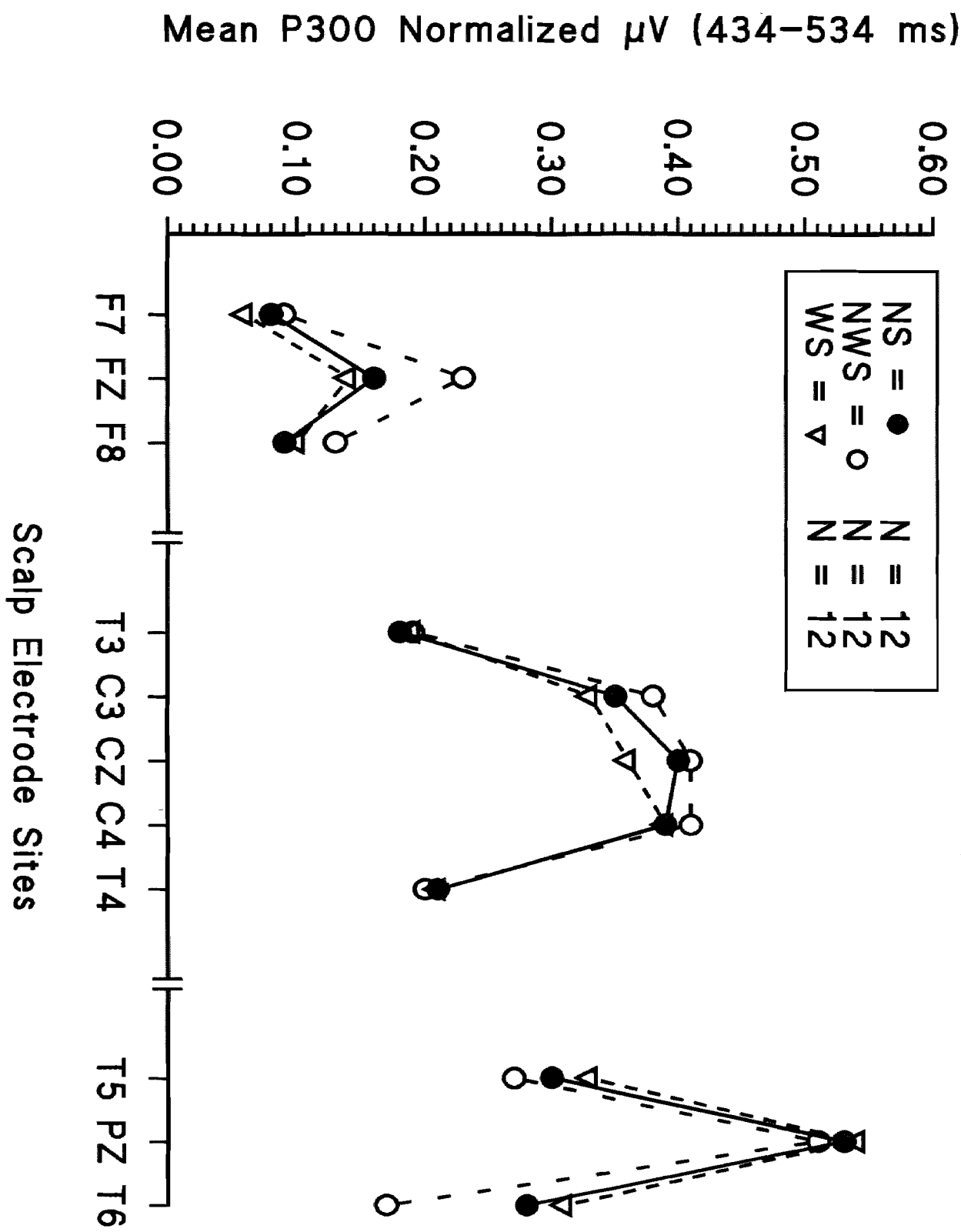

Mean P300 Normalized μV (434–534 ms)
0.00
0.10
0.20
0.30
0.40
0.50
0.60
NS = ● N = 12
NWS = o N = 12
WS = Δ N = 12
F7 FZ F8
T3 C3 CZ C4 T4
T5 PZ T6
Scalp Electrode Sites

Figure 4. Mean P300 Normalized Amplitude Values Averaged across Session 1 and Session 2 for Nonsmokers, Nonwithdrawn Smokers, and Withdrawn Smokers.

P300 Latency Analyses Mean P300 latencies among the midsagittal chain of electrodes (Fz, Cz, and Pz) are presented in Table 7. A planned three-factor model ANOVA, with "site" and "session" as the within-subject variables and "group" as the between-subject variable, was conducted, however, there were no statistically significant main effects or interactions.

TABLE 7

Midsagittal P300 Latencies for Nonsmoking, Nonwithdrawn, and Withdrawn Subjects

Group	Session 1 Sites			Session 2 Sites		
	FZ	CZ	PZ	FZ	CZ	PZ
	P300 Latencies (ms)					
Controls						
Mean	483.33	490.08	483.58	482.67	480.25	464.50
SD	(31.67)	(35.06)	(33.44)	(30.19)	(29.38)	(26.10)
Nonwithdrawns						
Mean	485.67	495.92	497.00	485.50	487.50	491.67
SD	(39.66)	(41.50)	(47.00)	(39.08)	(41.77)	(41.99)
Withdrawns						
Mean	485.25	506.17	498.67	475.00	476.17	490.00
SD	(34.37)	(36.85)	(30.47)	(42.37)	(39.98)	(32.15)

Exploratory Spearman Rank (rho) Correlational Analyses

Pz P300 Amplitude and Smoking Variables Spearman ranked correlational analyses were performed between the WS and NWS groups' smoking variables and integrated non-normalized Pz amplitude (as Pz produced the largest P300 amplitude and variance at any scalp site) using 2-tailed t-tests. These correlations are presented in Table 8. The number of cigarettes smoked on break between the two sessions did not appear to be statistically related to Pz amplitude. However, there may be a weak negative correlation with the second session Pz amplitude (rho = -.351, $p < .06$). Moreover, there was no significant correlation between Pz amplitude and CO levels or Pz amplitude and duration of smoking (years), indicating that there was no relationship between P300 amplitude and CO or the duration of smoking. There were only two smoking variables to statistically correlate with P300 Pz amplitude: the number of puffs the smokers took while smoking on break between the sessions (session 1: rho = -.501, $p < .05$; session 2: rho = -.514, $p < .01$), and cigarette tar levels, which correlated with the first session Pz amplitude (rho = .446, $p < .05$) but not with second session Pz amplitude ($p > .05$).

Table 8

Exploratory Two-Tailed Spearman Ranked Correlations for Nonwithdrawn and Withdrawn Smoking Groups' P300 Pz Integrated Amplitude (434-534 ms) with Smoking Variables for Session 1 and Session 2

	Session 1 Pz Amplitude	Session 2 Pz Amplitude
Duration Cigarette Use (yrs)	r = .319	r = .006
Number Cigarettes Consumed While on Break	r = -.185	r = -.351
Number Puffs Taken While on Break	r = -.501**	r = -.514**
Nicotine (mg)/Cigarette	r = .341	r = .189
Tar (mg)/Cigarette	r = .446*	r = .290

Table 8 (cont'd)	Session 1 Pz Amplitude	Session 2 Pz Amplitude
Pre-smoking CO (ppm)	r = -.148	r = .018
Post-smoking CO (ppm)	r = -.274	r = -.186
Pre-smoking Subjective State Questionnaire	r = -.066	r = -.325
Post-smoking Subjective State Questionnaire	r = -.265	r = -.274

Note: * = $p < .05$, ** = $p < .01$

Additionally, when using subjects from all three groups, there were no significant correlations between Pz amplitude and amount of alcohol consumed per week, duration of alcohol use ($p > .05$), or duration of illegal drug use ($p > .05$).

B" and Smoking Variables Spearman ranked correlations were performed between the response measure, B", and the smoking measures for the NWS and WS groups. The first session's first block B" measurement was significantly correlated with pre-smoking CO levels for both NWS (rho = -.66, $p < .05$) and WS (rho = -.60, $p < .05$), while the post-smoking CO measurement was significant for the NWS group (rho = -.59, $p < .05$) but not the WS group ($p > .05$). This same measure of B" was also significantly correlated with the number of puffs taken on break for the NWS group (rho =-.60, $p < .05$), but not the WS group ($p > .05$). Although not statistically significant, there was a trend for the cigarette nicotine content to be related to the WS group's first session first block B" and second session's second block B" (rho = -.55, $p = .065$; rho = -.59, $p = .054$ respectively).

CHAPTER IV

DISCUSSION

P300 Components P300 amplitudes statistically differed between nonsmokers (NS), nonwithdrawn smokers (NWS), and withdrawn smokers (WS) using a degraded visual continuous performance task (CPT). As presented in Figure 2, P300 amplitude showed a main effect of group and a group x site interaction, primarily produced by group differences at posterior scalp electrode sites. More specifically, the smoking groups (WS, NWS), overall, had smaller P300 amplitudes in posterior scalp regions than the nonsmoking group (NS). Effects of "session" were not found. Note that both smoking groups consistently had lower P300 amplitudes at each electrode site, both before and after smoking on break, the exception being in the frontal region where nonwithdrawn smokers had the overall largest P300 amplitudes. Moreover, the withdrawn group's midline P300 amplitudes did not statistically differ from session one to session two. This may indicate that smoking for 15 minutes after abstaining from smoking for 12 hours was not sufficient to raise withdrawn smokers' P300 amplitudes to their "normal" level.

A topographic difference was also present between the three groups such that NWS group had the largest normalized P300 amplitudes in the frontal and central regions of the scalp, followed by the NS and WS groups; an inverted pattern was revealed in the posterior region. Asymmetries were also present within groups. For example, the NWS group's T6 electrode, located in the right-temporal region, had a much lower normalized P300 amplitude than the T5 electrode, similarly situated on the left side of the scalp.

Taken together, this study suggests that P300 amplitude is not modulated in smokers by short-term alterations in blood-nicotine content or other products of tobacco smoke alone. While the two smoking groups showed similar P300 amplitude values in the posterior region of the scalp, they differed from one another in the frontal and central regions of the scalp. This may suggest that 12 hours of cigarette deprivation may be time enough to alter P300 topography, indicating differences in P300 brain generators. In addition, the overall group amplitude differences between smokers and nonsmokers also suggests the possibility that P300 amplitude

may be affected by the long-term effects of smoking. If so, the physiologic explanation does not necessarily reside in the long-term consumption of nicotine. Smoke condensate contains many substances, including CO, which reduce lung capacity and blood-oxygen. Smokers, therefore, are exposed to slight but prolonged deprivation, which may ultimately affect information processing and perhaps the P300 ERP. Firm conclusions cannot be obtained from this study, since smokers differ from nonsmokers on numerous dimensions, including a greater risk for substance abuse.

Questions may have been raised about possible confounds resulting in P300 amplitude differences between the three groups (i.e., substance abuse). However, we believe that the P300 amplitude and topographical differences between the three groups are due to differences in smoking. The reasons for this conclusion are as follows: 1) there were no significant correlations between illegal drugs or alcohol and the major dependent variable, P300 amplitude, between the three groups; 2) there were no significant correlations between carbon monoxide levels and P300 Pz amplitudes between the two smoking groups. (Moreover, past research has shown that CO has little or no psychological effects at smoking doses, while nicotine is pharmacologically the most potent agent in cigarette smoke [Guillerm, Radziszewski, & Caille, 1978; Wesnes & Warburton, 1978; for further review see Warburton, 1990]). However, over the long term, smokers differ from nonsmokers on CO content as well as various other cigarette chemicals; 3) there was a significant negative correlation between the number of cigarette puffs taken on break and P300 amplitude for both sessions one and two; and finally 4) the two smoking groups did not differ in the amount of cigarettes smoked per week, the amount of nicotine and tar contained within each cigarette smoked, nor the amount of cigarettes and puffs taken on break. Therefore, between the two smoking groups, the only known difference affecting the P300 ERPs was the condition of being withdrawn or nonwithdrawn from cigarettes for 12 hours. The only known difference affecting the P300 ERPs between the nonsmokers and smokers was the condition of smoking or not. There is a possibility that personality differences exist between nonsmokers and smokers which may confound the ERP results. However, we think personality differences are an unlikely confound, given that there are few known correlates of P300

components and personality factors. Therefore, the differences in P300 amplitude between groups are more likely the direct result of smoking status. Future studies should examine this issue.

Behavioral Measures In addition to P300 differences, the three groups also differed on two behavioral measures : hit rate and response bias. Both the NS and NWS groups' hit rate, averaged across blocks, increased across the two sessions. In contrast, the WS group's hit rate decreased during the second session. As predicted, each groups' hit rate declined over time within each session, presumably due to fatigue factors.

Interestingly, response bias differentiated the three groups. This measure was, however, considered exploratory because few smoking studies have investigated it. Nonsmokers and withdrawn smokers had virtually the same liberal response bias in session one relative to the nonwithdrawn smoker's more conservative bias. During the second session, after smoking, the withdrawn smoker's response bias was virtually identical to the nonwithdrawn smoker's response. Nonsmokers, in contrast, became more liberal responders during the second session, suggesting that this group "preferred" to commit the error of false-alarms rather than misses. One of the few previous studies which examined response bias in relation to nicotine did not find group differences in B" between young normal controls, elderly normal controls, and an AD group given nicotine using a visual computerized task (Sahakian et al., 1989). One important point to note is that if there is indeed a trend for B" to differentiate between smokers and nonsmokers, previous studies which only measured hit rate may have confounded perceptual sensitivity (A') with response bias (B"). Response bias will be an important variable for future smoking studies to investigate.

The only behavioral measure to statistically differ between sessions for the WS group was FA rate, which was twice as large in the first session than the second session (.04 to .02). This suggests that during the first session the WS group preferred to commit the error of "false-alarms", responding more often than necessary, rather than "miss". However, during the second

session WSs preferred to respond less often, preferring to commit the error of "miss" rather than "false-alarms".

General Conclusions In sum, P300 amplitude and topography differences were found to exist between NS, NWS, and WS groups. Although prior studies have reported P300 differences between smokers and nonsmokers, this study fills a void in the literature for the following reasons. First, the current study found that smoking is associated with P300 amplitude reduction, although not P300 prolongations as found in previous studies (i.e., Wesnes & Warburton, 1978,1983; Edwards & Warburton, 1983; Edwards et al., 1985) nor reaction time delays (i.e., Wesnes & Warburton, 1978, 1983). The current study did, however, replicate and extend the findings of Knott (1985) who found no significant effects of tobacco on RT using forced pacing of time and number of puffs. Previous studies (i.e., Warburton & Wesnes, 1984; Wesnes & Warburton, 1983) found that nicotine had no effect on response bias, but instead counteracted decrements in stimulus sensitivity. The current study stands in contrast, as it found that smoking affected B", but not A'.

Finally, we believe this is the first study to investigate P300 topography as it relates to smoking. Although, the three groups' P300 differed with nonsmokers having the overall largest P300 amplitudes followed by nonwithdrawn smokers and withdrawn smokers respectively; the nonwithdrawn smokers had statistically higher normalized P300 amplitudes at the frontal and central electrodes than either the nonsmokers or withdrawn smokers. An inverted P300 amplitude pattern was found in the posterior region where withdrawn smokers had the highest normalized P300 amplitudes followed by the nonsmokers and nonwithdrawn smokers respectively. Taken together these findings suggest that the smokers' and nonsmokers' P300 topographies differ, perhaps due to the effects of nicotine acting either directly or indirectly upon P300 temporal lobe generators. Preliminary evidence also suggests that the nonwithdrawn smoker's topography differs from withdrawn smoker's which may be due to subtle changes in neurotransmitter levels.

The fact that this study did not replicate previous studies' reaction time and P300 latency differences between groups may be due to differences in subjects (i.e. gender, age, number, their smoking duration, frequency, cigarette nicotine content, etc.), experimental design (i.e. auditory vs. visual), stimuli themselves (numbers vs. letters, nondegraded vs. degraded), task demands (pushing response button vs. silently counting strings of odd/even digits), time to complete paradigm), or perhaps the time from nicotine intake to task completion. It has been well documented that the time of testing following smoking is crucial because the blood levels of nicotine rise rapidly during smoking, reach a peak immediately after the last puff, and then decline rapidly often to less that 50% in 10 minutes (Wesnes & Warburton, 1984). In the current study, each subject was given a 15 minute break between sessions. During this time, smokers varied in their cigarette consumption, as they were told to "smoke until satisfied". For example, one smoker may have smoked a cigarette during the first five minutes and then relaxed for the remaining 10 minutes, whereas a second smoker may have smoked numerous cigarettes throughout the 15 minute break. Thus, there was subject variation in the number of cigarettes and time from last cigarette puff to second CPT task, which in some cases could have exceeded 10 minutes. Therefore, studies which have reported significant P300 latency and reaction time differences may have measured subjects either during or immediately after smoking.

Future studies should make every attempt to control the time from nicotine intake to onset of the experiment as well as analyze nicotine intake with greater precision. For example, variables such as puff duration, nicotine butt analysis, inter-puff interval, puff volume, butt length, butt nicotine analysis, percent tobacco burned, cigarette duration, salivary nicotine level, plasma cotinine and nicotine level were all measures recommended by Edwards and Warburton (1984), but unfortunately were beyond the scope of this study. Additionally, it would be beneficial for future studies to record EEG while subjects smoke to obtain immediate effects of smoking.

The results of the current study are preliminary and should be treated as such until [illegible] We invite other researchers to examine P300 topography as it relates to smoking and

to utilize the degraded visual CPT, encouraging them to take into account current alcohol and illegal drug usage of subjects (as was done in the present study) since these substances have been strongly correlated with cigarette usage (Istavan & Matarazzo, 1984) and may inadvertently confound ERP results. Finally, we encourage future studies to adopt the present study's experimental design, because it allows for signal-detection theory making it possible to measure both perceptual sensitivity and response bias. Previous studies did not always measure B" and therefore may have confounded B" and A'. Future studies will need to examine the relationship of smoking and B". The present study's experimental design is also unique in that it allows for both between- and within-subject comparisons. Within-subject comparisons are important in that they help to alleviate between-subject variability and allow for more direct comparisons (Wesnes & Warburton, 1984). Within-subject comparisons of withdrawn smokers will be crucial in the future to aid in our understanding of short-term effects of smoking.

REFERENCES

Aaronson, D., & Watts, B. (1987). Extension of Grier's computational formula for A' and B" to below-chance performance. Psychological Bulletin, 102, 439-442.

American Psychiatric Association. (1987). Diagnostic and statistical manual of mental disorders. (3rd ed. rev.). Washington, DC.: American Psychiatric Association.

Araujo, D.M., Lapchak, P.A., Collier, B., & Quirion, R. (1988). Characterization of [3H]*N*-methylcarbamylcholine binding sites and effect of *N*-methylcarbamylcholine on acetylcholine release in rat brain. Journal of Neurochemistry, 51, 292-299.

Armitage, A.K., Hall, G.H., & Morrison, C.F. (1968). Pharmacological basis for the tobacco smoking habit. Nature, 217, 331-334.

Balfour, D.J.K. (1982). The effects of nicotine on brain neurotransmitter systems. Pharmacology and Therapeutics, 16, 269-282.

Benowitz, N.L., Porchet, H., & Jacob, P., III. (1990). Pharmacokinetics, metabolism, and pharmacodynamics of nicotine. In S. Wonnacott, M.A.H. Russell, & I.P. Stolerman (Eds.), Nicotine psychopharmacology: Molecular, cellular, and behavioral aspects (pp. 158-193). Oxford: Oxford University Press.

Benwell, M.E.M., Balfour, D.J.K., & Anderson, J.M. (1988). Evidence that tobacco smoking increases the density of (-) [3H]-nicotine binding sites in human brain. Journal of Neurochemistry, 50, 1243-1247.

Callaway, E. (1984). Human information processing: Some effects of methylphenidate, age, and scopolamine. Biological Psychiatry, 19, 649-662.

Callaway, E., Halliday, R., Naylor, H., & Schecter, G. (1985). Effects of scopolamine on human stimulus evaluation. Psychopharmacology, 85, 133-138.

Chiou, C.Y. (1973). Mechanism of acetylcholine release by drugs and its blockade. Archives Internationales de Pharmacodynamie et de Therapie, 201, 170-181.

Chiou, C.Y., & Long, J.P. (1969). Acetylcholine-releasing effects of some nicotinic agents on chick biventer cervias muscle preparation. Proceedings of the Society for Experimental Biology and Medicine, 132, 732-737 .

Cinciripini, P.M. (1986). The effects of smoking on electrocortical arousal in coronary prone (Type A) and non-coronary prone (Type B) subjects. Psychopharmacology, 90, 522-527.

Clarke, P.B.S. (1987). Recent progress in identifying nicotinic cholinoreceptors in mammalian brain. Trends in Pharmacological Sciences, 8, 32-35.

Clarke, P.B.S. (1990). The central pharmacology of nicotine: electrophysiological approaches. In S. Wonnacott, M.A.H. Russell, & I.P. Stolerman (Eds.), Nicotine psychopharmacology: Molecular, cellular and behavioral aspects (pp. 158-193). Oxford: Oxford University Press.

Clarke, P.B.S., & Pert, A. (1985). Autoradiographic evidence for nicotine receptors on nigrostriatal and mesolimbic dopaminergic neurons. Brain Research, 348, 355-358.

Clarke, P.B.S., Hamill, G.S., Nadi, N.S., Jacobowitz, D.M., & Pert, A. (1986). [3H]-nicotine and [125I]alpha-bungarotoxin-labeled nicotinic receptors in the interpenduncular nucleus of rats II. Effects of habenular deafferentation. Journal of Comparative Neurology, 251, 407-413.

Clarke, P.B.S., Pert, C.B., & Pert, A. (1984). Autoradiographic distribution of nicotine receptors in the brain. Brain Research, 323, 390-395.

Clarke, P.B.S., Schwartz, R.D., Paul, S.M., Pert, C.B., & Pert, A. (1985). Nicotinic binding in rat brain: autoradiographic comparison of [3H]acetylcholine, [3H]nicotine and [125I]alpha-bungarotoxin. Journal of Neuroscience, 5, 1307-1315.

Costa, L.G., & Murphy, S.D. (1983). [3H]-nicotine binding in rat brain: alteration after chronic acetylcholinesterase inhibition. Journal of Pharmacology and Experimental Therapeutics, 226, 392-397.

Domino, E.F. (1967). Electroencephalographic and behavioral arousal effect of small doses of nicotine: A neuropsychopharmacological study. Annals of the New York Academy of Sciences, 142, 216-244.

Domino, E.F. (1986). Nicotine: A unique psychoactive drug - arousal with skeletal muscle relaxation. Psychopharmacology Bulletin, 22(3), 870-874.

Donchin, E. (1979). Event-related potential: a tool in the study of human information processing. In H. Begleiter (Ed.), Evoked brain potentials and behavior (pp. 13-88). New York: Plenum Press.

Donchin, E. (1981). Surprise! . . . Surprise! Psychophysiology, 18, 493-513.

Donchin, E. (1984). Dissociation between electrophysiology and behavior - a disaster or a challenge? In E. Donchin (Ed.), Cognitive psychophysiology. Hillsdale, New Jersey: Lawrence Erlbaum.

Donchin, E., & Fabiani, M. (1991). The use of event-related brain potentials in the study of memory: Is P300 a measure of event distinctiveness? In J.R. Jennings & M.G.H. Coles (Eds.), Handbook of cognitive psychology (pp. 471-498). New York: John Wiley & Sons.

Donchin, E., et al. (1978). Cognitive psychophysiology: The endogenous components of the ERP. In E. Calloway et al. (Eds.), Event-related potentials in man (pp. 349-441). Orlando, FL: Academic Press.

Edwards, J.A., & Warburton, D.M. (1983). Smoking, nicotine and electrocortical activity. Pharmacology and Therapeutics, 19, 147-164.

Edwards, J.A., & Warburton, D.M. (1984). Smoking, nicotine and electrocortical activity. In D.J.K. Balfour (Ed.), International encyclopedia of pharmacology and therapeutics section 114; nicotine and the tobacco smoking habit. Oxford: Pergamon Press.

Edwards. J.A., Wesnes, K., Warburton, D.M., & Gale, A. (1985). Evidence of more rapid stimulus evaluation following cigarette smoking. Addictive Behaviors, 10, 113-126.

Fagerström, K.O. (1978). Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addictive Behaviors, 3, 235-241.

Fagerström, K.O. (1983). Tolerance, withdrawal and dependence on tobacco and smoking termination. International Review of Applied Psychology, 32, 29-32.

Golding, J.F. (1988). Effects of cigarette smoking on resting EEG, visual evoked potentials and photic driving. Pharmacology Biochemistry & Behavior, 29, 23-32.

Goodin, D.S., Squires, K.C., & Starr, A. (1978). Long-latency event-related components of the auditory evoked potential in dementia. Brain, 101, 635-648.

Green, D.M., & Swets, J.A. (1966). Signal detection theory and psychophysics. New York: Wiley.

Grier, J.B. (1971). Formulae for a non-parametric index of sensitivity. Psychological Bulletin, 75, 424-429.

Guillerm, R., Radziszewski, E., & Caille, J.E. (1978). Effects of carbon monoxide on performance in a vigilance task (automobile driving). In R.E. Thornton (Ed.), Smoking behaviour: Physiological and psychological influences. Edinburg: Churchill Livingstone.

Halgren, E.J., Squires, N.K., Wilson, C.L., Rohrbaugh, J.W., Babb, T.L., & Crandall, P.H. (1980). Endogenous potentials generated in the human hippocampal formation and amygdala by infrequent events. Science, 210, 803-805.

Halgren, E., Stapleton, J.M., Smith, M., & Altafullah, I. (1986). Generators of the human scalp P3(s). In R.Q. Cracco & I. Bodis-Wollner (Eds.), Evoked potentials (pp. 269-284). New York, Alan Liss.

Hall, G.H. (1970). Effects of nicotine and tobacco smoke on electrical activity of cerebral cortex and olfactory bulb. British Journal of Pharmacology, 38, 271-286.

Hammond, E.J., Meador, K.J., Aung-Din, R., & Wilder, B.J. (1987). Cholinergic modulation of human P3 event-related potentials. Neurology, 37, 346-350.

Henningfield, J.E., & Jasinski, D.R. (1983). Human pharmacology of nicotine. Psychopharmacology Bulletin, 19, 412-415.

Hillyard, S.A., & Kutas, M. (1983). Electrophysiology of cognitive processing. Annual Reviews of Psychology, 34, 33-61.

Istavan, J., & Matarazzo, J.D. (1984). Tobacco, alcohol, and caffeine use: A review of their interrelationships. Psychological Bulletin, 95(2), 301-326.

Jaffe, J.H. (1990). Tobacco smoking and nicotine dependence. In S. Wonnacott, M.A.H. Russell, & I.P. Stolerman (Eds.), Nicotine psychopharmacology: Molecular, cellular, and behavioural aspects (pp. 1-36). Oxford: Oxford University Press.

Jarvis, M.J., Belcher, M., Vesey, C., & Hutchison, D.C.S. (1986). Low cost carbon monoxide monitors in smoking assessment. Thorax, 41, 886-887.

Jarvis, M.J., Transtall-Pedoe, H., Feyerabend, C., Vesey, C., & Saloojee, Y. (1987). Comparison of tests used to distinguish smokers from non-smokers. American Journal of Public Health, 77(11), 1435-1438.

Jasper, H.H. (1958). The ten-twenty electrode system of the International Federation. Electroencephalogram and Clinical Neurophysiology, 10, 371-375.

Kellar, K.J., & Wonnacott, S. (1990). Nicotinic cholinergic receptors in Alzheimer's disease. In S. Wonnacott, M.A.H. Russell, & I.P. Stolerman (Eds.), Nicotine psychopharmacology: Molecular, cellular, and behavioural aspects (pp. 341-373). Oxford: Oxford University Press.

Knight, R.T. (1990). Neural mechanism of event-related potentials: evidence from human lesion studies. In J.W. Rohrbaugh, R. Parasuraman, & R. Johnson, Jr. (Eds.), Event related brain potentials: Basic issues and applications. (pp. 3-18). New York: Oxford University Press.

Knott, V.J. (1985). Effects of tobacco and distraction on sensory and slow cortical evoked potentials during task performance. Neuropsychobiology, 13, 136-140.

Knott, V.J., & De Lugt, D. (1991). Subjective and brain-evoked responses to electrical pain stimulation: effects of cigarette smoking and warning condition. Pharmacology, Biochemistry, & Behavior, 39, 889-893.

Knott, V.J. & Venables, P.H. (1977). EEG alpha correlates of non-smokers, smoking and smoking deprivation. Psychophysiology, 14, 150-156.

Kutas, M., McCarthy, G., & Donchin, E. (1977). Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. Science, 197, 792-795.

Lichtensteiger, W., Dominiak, F., Lienhart, R., & Hefti, F. (1976). A quantitative correlation between single unit activity and fluorescence intensity of dopamine neurons in zona compacta of substantia nigra, as demonstrated under the influence of nicotine and physostigmine. Brain Research, 117, 85-103.

London, E.D., Waller, S.B., & Wamsley, J.K. (1985). Autoradiographic localization of [3H]nicotine binding sites in the rat brain. Neuroscience Letters, 53, 179-184.

Marks, M.J., Burch, J.B., & Collins, A.C. (1983). Effects of chronic nicotine infusion on tolerance development and nicotine receptors. Journal of Pharmacology and Experimental Therapeutics, 226, 817-825.

Marks, M.J., Stitzel, J.A., & Collins, A.C. (1985). Time course study of the effects of chronic nicotine infusion on drug response and brain receptors. Journal of Pharmacology and Experimental Therapeutics, 235, 619-628.

Marks, M.J., Stitzel, J.A., Romm, E., Wehner, J.M., & Collins, A.C. (1986). Nicotinic binding sites in rat and mouse brain: comparison of acetylcholine, nicotine and alpha-bungarotoxin. Molecular Pharmacology, 31, 169-174.

McCarley, R.W., Faux, S.F., Shenton, M.E., Nestor, P.G., & Adams, J. (1991). Event-related potentials in schizophrenia: Their biological and clinical correlates and a new model of schizophrenic pathophysiology. Schizophrenia Research, 4, 209-231.

McCarley, R.W., Shenton, M.E., O'Donnell, B.F., Faux, S.F., Kikinis, R., Nestor, P.G., & Jolesz, F.A. (1993). Auditory P300 abnormalities and left posterior superior temporal gyrus volume reduction in schizophrenia. Archives of General Psychiatry, 50, 190-197.

McCarthy, G., & Donchin, E. (1981). A metric for thought: A comparison of P300 latency and reaction time. Science, 211, 77-80.

McCarthy, G., & Wood, C.C. (1985). Scalp distributions of event-related potentials: An ambiguity associated with analysis of variance models. Electroencephalography and Clinical Neurophysiology, 62, 203-208.

Meador, K.J., Loring, D.W., Adams, R.J., Patel, B.R., Davis, H., & Hammond, E.J. (1987). Central cholinergic systems and the P3 evoked potential. International Journal of Neuroscience, 33, 199-206.

Meador, K.J., Loring, D.W., Davis, H.C., Sethi, K., Patel, B., Adams, R., & Hammond, E. (1989). Cholinergic and serotonergic effects on the P3 potential and recent memory. Journal of Clinical and Experimental Neuropsychology, 11, 252-260.

Meador, K.J., Loring, D.W., Lee, G.P., Taylor, H.S., Hughes, D.R., & Feldman, D.S. (1988). In vivo probe of central cholinergic systems. Journal of Gerontology, 43,158-162.

Nestor, P.G., Faux, S.F., McCarley, R.W., Sands, S.F., Horvath, T.B., & Peterson, A. (1991). Neuroleptics improve sustained attention in schizophrenia. Neuropsychopharmacology, 4, 145-149.

Nestor, P.G., Faux, S.F., McCarley, R.W., Shenton, M.E., Sands, S.F. (1990). Measurement of visual sustained attention using signal detection analysis and a newly-developed computerized CPT task. Schizophrenia Research, 3, 329-332.

Nobilio, D., Faricelli, A., Colangelo, U., Delre, M.L., Bazzano, S., Onofrj, M., & Gambi, D. (1990). The effect of levo-acetyl-carnitine on P300 potential. Current Therapeutic Research, 47(2), 267-277.

Nuechterlein, K.H., Parasuraman, R., & Jiang, Q. (1983). Visual sustained attention and image degradation produces rapid sensitivity decrement over time. Science, 14, 323-326.

O'Connor, K.O. (1982). Individual differences in the effect of smoking on frontal-central distribution of the CNV: Some observations on smokers' control of attentional behavior. Personality and Individual Differences, 3, 271-285.

O'Donnell, B.F., Friedman, S., Squires, N.K., Maloon, A., Drachman, D.A., & Swearer, J.M. (1990). Active and passive P3 latency in dementia. Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 3(3), 164-179.

O'Donnell, B.F., Friedman, S., Swearer, J.M., & Drachman, D.A. (1992). Active and passive P3 latency and psychometric performance: influence of age and individual differences. International Journal of Psychophysiology, 12, 187-195.

O'Donnell, B.F., Squires, N.K., Martz, M.J., Chen, J., & Phay, A.J. (1987). Evoked potential changes and neuropsychological performance in Parkinson's disease. Biological Psychology, 24, 23-37.

Oldfield, R.C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia, 9, 97-114.

Parasuraman, R. (1984). Sustained attention in detection and discrimination. In R. Parasuraman, & D.R. Davies (Eds.), Varieties of attention (pp. 243-267). Orlando, FL: Academic Press.

Perry, E.K., Perry, R.H., Smith, C.J., Dick, D.J., Candy, J.M., Edwardson, J.A., Fairbairn, A., & Blessed, J.G. (1987). Nicotinic receptor abnormalities in Alzheimer's and Parkinson's diseases. Journal of Neurology, Neurosurgery and Psychiatry, 50, 806-809.

Pfefferbaum, A., Ford, J.M., Roth, W.T., & Kopell, B.S. (1980). Age-related changes in auditory event-related potentials. Electroencephalography and Clinical Neuropsychology, 49, 266-276.

Pfefferbaum, A., Wenegart, B.G., Ford, J.M., Roth, W.T., & Kopell, B.S. (1984). Clinical application of the P3 component of event-related potentials. I. Normal aging. II. Dementia, depression, and schizophrenia. Electroencephalography and Clinical Neuropsychology, 59, 85-124.

Pickworth, W.B., Herning, R.I., & Henningfield, J.E. (1986). Electroencephalographic effects of nicotine chewing gum in humans. Pharmacology Biochemistry and Behavior, 25, 879-

Picton, T.W., Campbell, K.B., Baribeau-Braun, J., & Proulx, G.B. (1978). The neurophysiology of human attention: A tutorial review. In J. Requin (Ed.), Attention and performance VIII. Hillsdale, NJ: Lawrence Earlbaum.

Pomerleau, O.R. (1986). Nicotine as a psychoactive drug: Anxiety and pain reduction, arousal, and appetite regulation. Psychopharmacology Bulletin, 22, 863-864.

Pomerleau, O.F., & Pomerleau, C.S. (1984). Neuroregulators and the reinforcement of smoking: Towards a biobehavioral explanation. Neuroscience & Biobehavioral Reviews, 8, 503-513.

Price, D.L. (1986). New perspectives on Alzheimer's disease. Annual Reviews of Neuroscience, 9, 489-512.

Price, D.L., Whitehouse, P.J., & Struble, R.G. (1985). Alzheimer's disease. Annual Reviews of Medicine, 36, 349-356.

Pritchard, W.S. (1981). Psychophysiology of P300. Psychological Bulletin, 89(3), 506-540.

Pritchard, W.S. (1991). Electroencephalographic effects of cigarette smoking. Psychopharmacology, 104, 485-490.

Pritchard, W.S., Duke, D.W., Coburn, K.L., & Robinson, J.H. (1991). Nonlinear dynamical electroencephalographic analysis applied to nicotine psychopharmacology and Alzheimer's disease. In P.M. Lipiello, A.C. Collins, J.A. Gray, & J.H. Robinson (Eds.), The biology of nicotine (pp. 195-215). New York: Raven Press, Ltd.

Rosvold, H.E., Mirsky, A., Sarason, I., Bransome, E.D., Jr., & Bech, H. (1956). A continuous performance test of brain damage. Journal of Consulting Psychology, 20, 343-350.

Rowell, P.P. (1987). Current concepts on the effects of nicotine in the central nervous system. In W.R. Martin, G.R. Van Loon, E.T. Iwamoto, & L. Davis (Eds.), Tobacco smoking and health (pp. 191-207). New York: Plenum Press.

Sahakian, B., Jones, G., Levy, R., Gray, J., & Warburton, D. (1989). The effects of nicotine on attention, information processing, and short term memory in patients with dementia of the Alzheimer type. British Journal of Psychiatry, 15, 797-800.

Schwartz, R.D. (1986). Autoradiographic distribution of high affinity muscarinic and nicotinic cholinergic receptors labeled with [3H]-acetylcholine in rat brain. Life Sciences, 38, 2111-2119.

Schwartz, R.D., Lehman, J., & Kellar, K.J. (1984). Presynaptic nicotinic cholinergic receptors labeled by [3H]acetylcholine on catecholamine and serotonin axons in brain. Journal of Neurochemistry, 42, 1495-1498.

Snyder, R.S., Davis, F.C., & Henningfield, J.E. (1989). The tobacco withdrawal syndrome: Performance decrements assessed on a computerized test battery. Drug and Alcohol Dependence, 23, 259-266.

Terry, R., & Katzman, R. (1983). Senile dementia of the Alzheimer type: Defining a disease. In R. Katzman, & R. Terry (Eds.), The neurology of aging. Philadelphia: Davis.

Ulett, J., & Itil, T. (1969). Qualitative electroencephalogram in smoking and smoking deprivation. Science, 164, 969-970.

Verleger, R. (1988). Event-related potentials and cognition: A critique of the context updating hypothesis and an alternative interpretation of P3. Behavioral and Brain Sciences, 11, 343-427.

Warburton, D.M. (1972). The cholinergic control of internal inhibition. In R.A. Boakes, & M.S. Halliday (Eds.), Inhibition and learning (pp. 431-460). London, England: Academic Press.

Warburton, D.M. (1990). Psychopharmacological aspects of nicotine. In S. Wonnacott, M.A.H. Russell, & I.P. Stolerman (Eds.), Nicotine psychopharmacology: Molecular, cellular, and behavioral aspects (pp. 77-111). Oxford: Oxford University Press.

Warburton, D.M., & Wesnes, K. (1978). Individual differences in smoking and attentional performance. In R.E. Thornton (Ed.), Smoking behaviour: Physiological and psychological influences (pp. 19-144). London: Churchill-Livingston.

Warburton, D.M., & Wesnes, K. (1984). Drugs as research tools in psychology: Cholinergic

Wesnes, K., & Warburton, D.M. (1978). The effects of cigarette smoking and attentional performance. In. R. E. Thornton (Ed.), Smoking behavior: Physiological and psychological influences. Edinburgh: Churchill Livingstone.

Wesnes, K., & Warburton, D.M. (1983). Smoking, nicotine, and human performance. Pharmacology and Therapeutics, 21, 189-208.

Wesnes, K., & Warburton, D.M. (1984). Smoking, nicotine and human performance. In D.J.K. Balfour (Ed.), International encyclopedia of pharmacology and therapeutics section 114: nicotine and the tobacco smoking habit (pp. 133-152). Oxford: Pergamon Press.

Whitehouse, P.J., Martino, A.M., Autuono, P.G., Lowenstein, P.R., Coyle, J.T., Price, D.L., & Kellar, K.J. (1986). Nicotinic acetylcholine binding in Alzheimer's disease. Brain Research, 371, 146-151.

Wonnacott, S. (1987). Brain nicotine binding sites. Human Toxicology, 6, 343-353.

Wonnacott, S. (1990). Characterization of nicotine receptor sites in the brain. In S. Wonnacott, M.A.H. Russell, & I.P. Stolerman (Eds.), Nicotine psychopharmacology: Molecular, cellular, and behavioral aspects (pp. 226-277). Oxford: Oxford University Press.

Woodson, P.P., Battig, K., Etkin, M.W., Kallman, W.M., Harry, G.J., Kallman, M.J., & Rosecrans, J.A. (1982). Effects of nicotine on the visual evoked response. Pharmacology Biochemistry and Behavior, 17, 915-920.

Yamada, S., Gehlert, D.R., Hawkins, K.M., Nakayama, K., Roeske, W.R., & Yamamura, H.I. (1987). Autoradiographic localization of nicotinic receptor binding in rat brain using [3H]methylcarbamylcholine, a novel ligand. Life Sciences, 41, 2851-2861.

Appendix A. DEMOGRAPHIC QUESTIONNAIRE

CODE: _____

1. How old are you? _____
2. Are you: MALE FEMALE
3. What is your dominant hand? RIGHT LEFT
4. Do you smoke? YES NO
5. If so, how many packs of cigarettes do you smoke a day? _____
6. How long have you smoked? _____
7. Do you consume alcohol? YES NO
8. What type of alcoholic beverage do you typically drink? (i.e. beer, wine, liquor) _____
9. How long have you been drinking alcohol? _____
10. How much of each alcoholic beverage do you typically drink in a week during the school year? _____
11. Do you drink caffeinated products? (i.e. coffee, tea, cola) YES NO
12. If so, how much of each caffeinated beverage do you typically drink in a week during the school year? _____
13. How long have you been drinking caffeinated products? _____
14. Do you have any history of neurological illness, head injury, or epilepsy? YES NO
15. If "YES", what disorders? _____
16. Are you currently taking any medications? YES NO
17. If "YES", what medications? _____
18. Do you currently use, or have you previously used, any recreational or psychoactive substances i.e.) marijuana, cocaine, heroin, etc.? YES NO
19. If "YES", list substances & frequency used _____
20. How long have you been using these substances? _____

Appendix B. FAGERSTRÖM TOLERANCE QUESTIONNAIRE
(Fagerström, 1978)

CODE: _____

1. How many cigarettes a day do you smoke? _____

2. What brand do you smoke? _____

3. Do you inhale? Always Sometimes Never

4. Do you smoke more during the morning than during the rest of the day? Yes No

5. How soon after you wake up do you smoke your first cigarette? _____

6. Which cigarette would you hate to give up? (Circle One)
   a) First of the day
   b) Middle of the day
   c) Last of the day

7. Do you find it difficult to refrain from smoking in places where it is forbidden, (i.e. in church, at the library, cinema, etc.?) _____

8. Do you smoke even when you are so ill that you are in bed most of the day? _____

Appendix C. DRUG SCREENING FOR 12 HOURS PRIOR TO P300 TESTING

CODE: _____

DATE: _____

Answer the following questions carefully, and honestly. You will not be penalized (lose extra credit) if you have used any of the following substances. It is of great importance that we are aware of your intake of the following items, as it could interfere and greatly affect the outcome of the present experiment.

1. Have you smoked within the last 12 hours? Yes No

2. If so, at what time did you last smoke? _____

3. How many cigarettes did you consume in the last 12 hours? _____

4. What brand did you smoke? _____

5. Have you chewed any nicotine gum in the last 12 hours? Yes No

6. Have you used a nicotine patch in the last 12 hours? Yes No

7. Have you used chewing tobacco in the last 12 hours? Yes No

8. How many cups of caffeinated coffee have you drank in the last 12 hours? _____

9. How much beer have you drank in the last 12 hours? _____

10. How much liquor have you drank in the last 12 hours? _____

11. Have you used any drugs (prescription or illegal) in the last 12 hours? Yes No

12. If so, what drugs and how many? _____

Appendix D. SUBJECTIVE QUESTIONNAIRE

Code: _____

Date: _____

Answer the following questions according to the way you feel right at this moment. Please read each question carefully and do not simply circle the same response for each question (i.e. circle all 7's or all 1's) unless it applies to you.

1. Currently, I feel the need for a cigarette:

1	2	3	4	5	6	7
not at all			moderately			extremely

2. Currently, I feel irritable:

1	2	3	4	5	6	7
not at all			moderately			extremely

3. Currently, I can concentrate well:

1	2	3	4	5	6	7
not at all			moderately			extremely

4. Currently, I feel tired:

1	2	3	4	5	6	7
not at all			moderately			extremely

5. Currently, I feel hungry:

1	2	3	4	5	6	7
not at all			moderately			extremely

6. Currently, I am in a bad mood:

1	2	3	4	5	6	7
not at all			moderately			extremely

(Appendix D cont'd)

7. Currently, I feel frustrated:

1	2	3	4	5	6	7
not at all			moderately			extremely

8. Currently, I feel alert:

1	2	3	4	5	6	7
not at all			moderately			extremely

9. Currently, I feel relaxed:

1	2	3	4	5	6	7
not at all			moderately			extremely

Appendix E. Edinburgh Handedness Inventory
Oldfield (1971)

CODE _____

Please indicate your preferences in the use of the hands in the following activities by *putting* + *in the appropriate column.* Where the preference is so strong that you would never try to use the other hand unless absolutely forced to, *put* ++. In any case where you are really indifferent, *put* + *in both columns.*

Some of these activities require both hands. In these cases the part of the task, or object, for which hand preference is wanted is indicated in parentheses.

Please try to answer all the questions, and only leave a blank if you have no experience at all of the object or task.

	Left	Right
1. Writing		
2. Drawing		
3. Throwing		
4. Scissors		
5. Toothbrush		
6. Knife (without fork)		
7. Spoon		
8. Broom (upper hand)		
9. Striking match (match)		
10. Opening box (lid)		